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ANNOUNCEMENT

IFTEEN years ago the American Journal of Obstetrics and Gynecology was launched as a successor to the American Journal of Obstetrics and Diseases of Women and Children, which had pursued an honorable and uninterrupted career of publication since 1868. The Great War as well as other factors had forced the suspension of the latter and left a hiatus with no medium devoted exclusively to this branch of medicine. The task of supplying the need for a journal to encompass the specialty seems to have been well met by the present publication, although the growth and interest of obstetrics and gynecology have made constantly increasing demands on its pages with resulting but unavoidable delays in publication. New societies which devote themselves to this specialty have likewise increased in number and importance, and their transactions constitute very valuable additions to medical literature society. During recent years it has been found necessary to condense discussions more and more until finally we were forced to suspend completely their publication. The earlier volumes of the Journal averaged about 800 pages while the last one includes almost 950. Even with this increase in the number of pages, original contributions had to be condensed and cut, and often bibliographies had to be omitted. High standards of acceptance have been adhered to and the contents of the Journal have included in cross-section contributions from all sources so far as it was possible to publish them within our page limits.

In response to the universal demand for more space, the editors and publishers of the Journal have decided to provide this by a substantial increase in the number of pages for each issue beginning with the January number, commemorating in this way the publication of the thirty-first volume. Each monthly issue will include an addition of 32 pages, or a total of about 200 pages per volume.

As announced in our initial prospectus "the American Journal of Obstetrics and Gynecology will be conducted by the profession for the profession and, in order that the latter may be fully represented in its management, the general conduct of the enterprise is vested in an Advisory Editorial Board, the membership of which serves as a guarantee that the interests of the profession will be adequately protected and assured." Various changes in the Advisory Editorial Board have been brought about by death and other reasons. Its members have been freely consulted in the acceptance or rejection of papers submitted for publication, and this practice will continue together with the more direct individual aid given by a special Publication Committee.

The editors and publishers again respectfully submit, as they did some fifteen years ago, the American Journal of Obstetrics and Gynecology to the attention and support of the profession, "fully realizing the trust imposed upon them and hoping for an endorsement of the attempt to serve their interests."

George W. Kosmak Hugo Ehrenfest

January 1, 1936.

Original Communications

CHRONIC HYPOCHROMIC ANEMIA IN WOMEN

A Consideration of Its Etiology and Treatment, with Special Reference to the Relationship of Gynecologic Disorders

LAMAN A. GRAY, M.D., AND M. M. WINTROBE, M.D., BALTIMORE, MD.

(From the Departments of Gynecology and Medicine, Johns Hopkins

Hospital and University)

TTENTION has been directed in recent years to a type of anemia which occurs almost exclusively in women, particularly between the ages of twenty and fifty years. The anemia is insidious in onset and of long duration. Symptoms of fatiguability, weakness, shortness of breath, palpitation, and gastrointestinal or nervous complaints are common, but in some instances the patients have become so adjusted to their state of poor health that, although they do not appear well, they deny any specific complaints. Some of these cases have been labelled "neurasthenic." On the other hand, such symptoms as glossitis, stomatitis, and paresthesias have led to the suspicion of pernicious anemia. In certain cases in which gynecologic symptoms have been prominent, surgical measures have been employed in treatment, but adequate attention has not been given to the other factors involved in the production of the anemia and relief of symptoms has consequently not been obtained. This anemia has been described under such titles as late chlorosis, simple achlorhydric anemia and idiopathic hypochromic anemia. Faber was one of the first to direct attention to this syndrome twenty-five years ago, but it was not until the papers of Witts² appeared that physicians commenced to recognize the condition. In the past five years a great number of reports have appeared. The most recent reviews are by Wintrobe and Beebe³ and by Bethell et al.4

The patients usually appear tired and lifeless. There is marked pallor in long standing eases, and this may be waxy or slightly yellowish in character. The scleras are usually quite blue or pearly white. The skin is often wrinkled and inelastic. The finger nails are usually dull and lusterless, longitudinally ridged, and may be actually concave instead of convex. There may be slight papillary atrophy of the tongue. Functional systolic murmurs in the heart are common. The liver may be palpable, and the spleen has been felt in almost 50

Note: The Editor accepts no responsibility for the views and statements of authors as published in their "Original Communications."

per cent of the cases. Although there may be complaints referable to the nervous system, objective neurologic findings are rarely if ever encountered.

The blood shows a marked reduction in hemoglobin which is quite out of proportion to the diminution in the number of red corpuscles. The latter, in fact, may be almost normal in number, even when the hemoglobin is greatly reduced. Considerable variation in the size of the red corpuscles is found in the blood smear, and some macrocytes may be observed, but the majority of the cells are small and poorly filled with hemoglobin. The mean volume of the corpuscles and their hemoglobin content³ are less than normal. Occasional normoblasts may be seen. No characteristic changes are found in the leucocytes or platelets. The anemia responds very readily to large doses of iron, but relapse is so common when iron is discontinued that it is considered to be characteristic.

The anemia is usually spoken of as being "idiopathic." Most writers have stressed the importance of achlorhydria in its etiology, while others have called attention to the importance of deficient diet. It has been noted that a number of these patients have undergone repeated pregnancies. Although it is generally recognized that menstrual disorders are common, they have usually not been considered as having an etiologic relation to the anemia.

Relatively few of the cases of idiopathic hypochromic anemia which have been reported have received adequate gynecologic study. Since the anemia encountered in these cases is indistinguishable from that due to chronic or repeated blood loss, both as regards morphologic characteristics and in its response to therapy, we felt that a careful consideration from the gynecologic standpoint, in addition to investigations of the gastric secretion and dietary habit, might afford important information in regard to the etiology of the anemia. The following observations are based on the study of forty cases which met the clinical and hematologic requirements³ for the diagnosis of idiopathic hypochromic anemia.

STUDY OF CASES

Myoma of the Uterus.—Myomas of the uterus were definitely palpable in eight (20 per cent) of the patients. All were associated with excessive uterine bleeding, which varied from menorrhagia confined to fairly regular periods of six to seven days, to menorrhagia at irregular periods which lasted two to three weeks. In four cases the diagnosis was confirmed at operation. None of the tumors were large; the supravaginal portion of the uterus removed at operation was only one and one-half to three times the size of the normal fundus. In addition to the eight patients with definite diagnoses of myomas of the uterus, there were two patients, included below under unexplained menorrhagia, in whom the excessive bleeding may well have been due to the same cause. The uterus in each of these individuals was diffusely enlarged, which suggests the presence of a myoma. Definite surface nodules were not felt, but the two patients would not permit examinations under anesthesia.

In seven of the eight cases, there was a definite history of menorrhagia preceding or coinciding with the development of symptoms of anemia. The eighth patient (A. R.) noted menorrhagia only after she had been treated with iron for ten months, during which time the hemoglobin had increased from 4.3 gm. (30 per cent) to 10.5 gm. (72 per cent). This menorrhagia persisted and there were frequent relapses, in spite of the fact that large doses of iron were prescribed. It is interesting to note that in this case and another (R. W.) when the hemoglobin became quite low, the menses were greatly diminished, but when the hemoglobin rose with the administration of large doses of iron, blood loss became greatly increased over the normal.

Five patients responded well to iron therapy, two fairly well and one poorly. In one of the latter three patients (H. Z.), phlebitis was thought to be responsible for the inadequate response. In two others (C. S. and R. M.), complete relief of the anemia was hindered by persisting menorrhagia. Curettage in one of these patients (C. S.) was followed by relief of menorrhagia and complete restitution of the blood to normal. Menorrhagia was not relieved in the other (R. M.), and she responded poorly to various forms of iron therapy. Finally fairly satisfactorily response followed the use of ferrous sulphate, in spite of continuing menorrhagia.

Relapses developed on discontinuation of iron in three cases (A. R., R. M. and R. W.). In all three of these patients, menorrhagia persisted. Hysterectomy was performed in four cases (H. Z., R. A., R. W. and C. S.) the blood having been first brought to normal or nearly normal with iron therapy. In these cases, after the iron was discontinued, the anemia did not recur in five, eight, nine and ten months respectively. In two patients (L. McC. and M. R.) the menopause occurred, iron was discontinued, and no relapse followed in ten and fourteen months, respectively.

Gastric achlorhydria after the histamine test was found in four of these cases, and, in three more, free hydrochloric acid failed to appear following the Ewald meal. In one patient the free hydrochloric acid following an alcohol test meal was fifteen.

Our patients were questioned in detail concerning their dietary habits. Special attention was paid to the intake of foods known for their hemoglobin producing effects, such as animal organs (liver, kidney, sweetbreads), animal skeletal muscle, fruits (especially apricots, peaches, and prunes), eggs, and green vegetables. Those who ate no animal protein or eggs, or at most took these foods rarely, were classified as taking a "very poor" diet. When these foods were eaten only once or twice a week, the patients were classified as taking a "moderately poor" diet. Any diet better than this was classified as "good."

Of the eight patients in whom myomas of the uterus were found, three took a diet very poor in iron-containing foods, two a moderately poor diet and three a good diet.

Endometrial Hyperplasia.—Cullen,⁵ followed by many others, has shown that hyperplasia of the endometrium is very commonly associated with menorrhagia and metrorrhagia. Five patients (12.5 per cent) in this series were found to have endometrial hyperplasia, as proved by examination of the curettings from the uterus in each case.

These patients stated that they had always been free bleeders, and had periods lasting seven to fourteen days. In each case there had been an increase in the menorrhagia just preceding the development of symptoms of anemia. One patient (A. T.) had always had menorrhagia, but with the development of marked weakness the menses for two years became scanty and of lighter color, and lasted only three to five days. The hemoglobin was 6.3 gm. (43 per cent) when she was first seen by us. As soon as the blood was brought to normal by iron, prolonged profuse menstrual periods reappeared and have continued for three years.

The blood of each of these individuals responded well to large doses of iron, except that of the patient who also had myomas of the uterus (H. Z.). In this

case the response was apparently delayed by phlebitis, as the blood later responded satisfactorily.

Relapse occurred in two cases (M. M. and F. P.) when iron was discontinued, but after menopause was produced by roentgen ray therapy, the blood was brought to normal by iron, and no relapse developed in four and eight months, respectively, after discontinuing iron. Curettage and then hysterectomy were performed in the case with submucous myomas and hyperplasia and the blood was brought to normal with iron. After the latter was discontinued there was no relapse in five months. One patient (A. T.) with continued menorrhagia has taken iron almost continuously for three years, and no relapse has developed. The fifth patient could not be followed.

Gastric achlorhydria after the histamine test was found in three cases. One patient showed free hydrochloric acid of 15 after an alcohol meal, and one free acid of 30 after the Ewald test meal.

Three patients took a very poor diet, one a moderately poor diet (H. K.) and one (M. M.) a good diet.

Unexplained Menorrhagia.—Fourteen patients (35 per cent) in this series have had excessive bleeding at the menstrual periods, and no cause has been found. (Small myomas have been suspected in two.) Six (15 per cent) of these have had moderate menorrhagia (profuse menses lasting seven to eight days) for several years or ever since puberty. In two of the latter, as the anemia progressed the menses diminished to a normal or even scant flow. Six (15 per cent) had marked menorrhagia (bleeding from eight to twenty-one days) preceding the onset of the anemia. In three of these the marked menorrhagia persisted throughout treatment of the anemia. One patient (S. M.) had always had moderate menorrhagia, but when the hemoglobin fell to 8.7 gm. (60 per cent), the menses became scant. Later when the blood was brought to normal, marked, instead of moderate menorrhagia appeared. The last (O. G.) of the fourteen patients with unexplained menorrhagia developed profuse prolonged periods after delivery, when the hemoglobin was 7.3 gm. (50 per cent). After several months the menorrhagia disappeared, to return a year later.

In only three of these patients has curettage been performed, the remainder having refused such an operation. Of the three, one showed chronic inflammation in premenstrual endometrium (both tubes had been removed, thus ruling out an incomplete abortion), and in two there was an early secretory type of endometrium. Very probably, if curettage could have been performed in the other cases, some would have shown hyperplasia or submucous myomas.

The blood of ten of these patients responded well to large doses of iron. That of one (O. G.) responded only fairly well but this was probably due to the fact that menorrhagia continued. Three patients have not been studied over a sufficient period of time.

When the iron was discontinued, there was relapse of the anemia in seven of the ten patients who have been followed. The menorrhagia had continued or returned in six, and the state of the menses was not known in the seventh case (L. W.). In three there was no relapse: one of these had passed the menopause; menstruation continued in one case but there was no longer any excessive flow; menorrhagia continued in the third patient, but large doses of iron were taken regularly and no relapse occurred.

Gastric achlorhydria was found in seven of this group (the histamine test was used in six). In one case (R. B.) free acid of two was found after an alcohol meal. In another patient (A. Y.) the free acid was ten after the Ewald meal. In three, normal acidity was found.

Ten of these patients were questioned about their diet. Two took a very poor diet, five a moderately poor one, and three a good diet.

Pregnancy.—The first appearance of symptoms of anemia in twelve (30 per cent) patients in this series was associated, according to the patient's own story, with pregnancy. Two of these patients (L. C. and E. Y.) were first seen by us during pregnancy, and in subsequent pregnancies relapse was observed. In the other ten cases the first actual blood examinations were made from three weeks to three years following pregnancy.

Six (15 per cent) of the above twelve cases, in addition to a history directly related to otherwise uncomplicated pregnancies, had had one or more abortions with hemorrhage, and two had had severe postpartum hemorrhages with subsequent pregnancies.

The blood of seven patients responded well to large doses of iron. One (M. P.) was pregnant, and her blood responded very slowly but it soon came to normal after delivery. The blood of another patient (O. G.) responded only fairly well, but she had marked menorrhagia. In the tenth patient (E. P.), sufficient time to study response has not yet elapsed. Two patients could not be followed.

The anemia relapsed in three patients during subsequent pregnancies. In two patients with marked menorrhagia there were relapses. In one (R. M.) there was no subsequent pregnancy and no menorrhagia; after the blood was brought to normal and the iron discontinued, there was no relapse in twelve months. One patient (L. W.) showed slight relapse during one year, but the state of the menses was not recorded. The remaining five patients have been observed an insufficient time to determine whether relapse will occur.

Two patients had seven pregnancies. In one they followed in rather rapid succession with increasing weakness and anemia. Three had six pregnancies, but the patients dated their symptoms of anemia from the last pregnancy. Two had four pregnancies; two, three; and three, two pregnancies.

Of these twelve patients, six had achlorhydria (five had histamine tests). One (H. A.) showed free acid of ten and another (L. C.) showed free acid of eighteen after histamine injection. Normal acid values were found in two cases.

Four patients in this group had taken very poor diets, four moderately poor, and two good diets.

No Gynecologic Condition.—In nine patients (22.5 per cent) in this series no abnormal blood loss at the menstrual periods was found, and the pelvic organs were normal. Although several of these patients had had one or more pregnancies, no definite relation of the history of the anemia to pregnancy or abortion could be found.

The ages of these patients varied from thirty-seven to sixty-six years, averaging forty-eight years. The menses had always been regular, except in one patient who had had slight irregularity. The periods in these cases lasted three to six days and never required more than two to three pads daily. Five patients had passed the menopause, sixteen, fourteen, twelve, seven, and three years previously. Six had had children, one as many as ten, but with one exception the last pregnancy varied from fourteen to forty years before the patients were seen. In one case there had been an abortion four years previously, but the blood was known to have been normal a year later.

The blood in each case responded well to large doses of iron. In five there was no relapse in from one to three years. In one (M. R.) after two years, during which she took no iron, there was a slight relapse. During this time she had not menstruated and had taken a good diet. The only factor to which we can attribute relapse of the anemia in this case is achlorhydria. One other patient (E. C.) developed menorrhagia for the first time in her life when the blood had been brought to normal. Rather marked relapse occurred in three months. This patient has achlorhydria and persists in her poor diet. The remaining two cases have been observed over too short a period to determine whether relapse will occur.

The diet was very poor in two cases, moderately poor in five, and good in two. Achlorhydria was found in six (histamine test used in all). One showed free hydrochloric acid of ten after an alcohol meal, one free acid of twelve after an Ewald meal and one normal acidity. The two patients with good diets had achlorhydria after the histamine test.

DISCUSSION

Blood loss at the menstrual periods which we considered in excess of the normal was present at some time, and usually for a considerable period of time, in twenty-seven (67.5 per cent) of our cases. In eight patients this was associated with small myomas of the uterus, in five with proved endometrial hyperplasia, and in fourteen the cause was not discovered. This incidence of menstrual disorder is much higher than has heretofore been recorded. In a review of the literature³ one of us found menorrhagia mentioned in only twenty-eight of 189 cases (15 per cent), but this represents a series of cases in which this symptom was not mentioned as well as groups in which it was specifically recorded. An example of the latter is Haden's series of thirty-three patients, among whom eleven complained of menorrhagia.

Our cases were selected only in the sense that the diagnosis of idiopathic hypochromic anemia was made by internists and the patients came to our attention because of their anemia rather than on account of gynecologic symptoms. We believe, therefore, that the great discrepancy between our findings and those recorded in the literature is due to the fact that few of the cases heretofore recorded have been specifically studied from the standpoint of the menstrual function, nor have most of them received a thorough examination by a gynecologist. Women are rarely precise in regard to statements concerning menstruation and unless they are carefully questioned about the quantity of blood lost, an inaccurate history is often obtained.

It may also be pointed out that the anemia in these cases frequently does not correspond with the degree of recent blood loss. It is essentially an anemia of many years' duration and excessive hemorrhage may have occurred a number of months previously, thus giving the impression that it was entirely unassociated with the anemia. Again, as the anemia becomes more pronounced the menstrual flow may become quite scanty. This was the case in six of our patients who gave a definite history of menorrhagia preceding the period of hypomenorrhea. It is significant also, that in four patients in whom the menstrual flow was normal or diminished at the time they were first seen, menorrhagia appeared when the anemia was relieved by iron therapy. It has not been our usual experience that menorrhagia, when present, is relieved by iron therapy, as is often stated.^{6, 7} In sixteen cases menorrhagia continued in spite of relief of the anemia.

TABLE I. SUMMARY OF CASES

	NUMBER	GASTRIC	GASTRIC ANALYSIS	О	DIET	G00D	RELAPSE A	RELAPSE ASSOCIATED WITH	RELAPSE FOLLOWING
GYNECOLOGIC	OF					KESP.	BLOOD	NO BLOOD	CHECKING OR
STATUS	CASES	ACHLOR- HYDRIA	HYPOCHLOR- HYDRIA	VERY	MOD. POOR	TO	LOSS OR PREGNANCY	LOSS OR PREGNANCY	BLOOD LOSS
Myomas of the uterus	00	1	1	3	CI	20	೧೦	0	None in 6
Endometrial hyperplasia	10	ಣ	1	cc	1	4	01	0	None in 4
Unexplained menorrhagia	14	2	C)	01	10	10	2	0	None in 6
Pregnancy, postpartum hemorrhage and abortion	12	9	ΦI	4	4	Ŀ	10	0	None in 3
Total cases with significant gyn.	500	19	10	10	œ	955	14	0	None in 16
No gyn. condition	6	9	01	©1	10	6	-	1	
Total	40	95	7	12	13	34	15	1	

The influence of pregnancy may be the same as that of blood loss, for hemoglobin-building material is probably withdrawn by the fetus.⁸ When to our group of cases with menorrhagia are added those in whom a definite relation to pregnancy, postpartum hemorrhage, or abortion could be found, the total number of cases in whom some form of blood loss was present becomes thirty-one (77.5 per cent). When it is considered that idiopathic hypochromic anemia occurs most often between the ages of twenty and fifty years, that there is a marked decrease in its incidence after fifty years of age,³ and that it is very rare in men, it seems reasonable to conclude that menstruation, pregnancy, and the associated disorders of a hemorrhagic nature are significant in the development of these cases of anemia.

It cannot be concluded, however, that blood loss is itself the sole cause of the anemia. In the normal individual the degree of blood loss which occurs in most of these cases does not cause anemia of the duration or severity encountered in idiopathic hypochromic anemia. Our own data support the assumption that a chronic defect in alimentary function and defective diet are important factors in the etiology of the anemia.

Achlorhydria as determined by the histamine test was found in twenty-one of our cases, and in four more there was no secretion of free hydrochloric acid following the Ewald meal. In seven patients there was hypochlorhydria, making a total of thirty-two of the thirty-eight cases examined (84 per cent) in whom some disturbance in gastric secretion was found. Using the histamine test, Polland⁹ found achlorhydria in 4.7 per cent, 7.5 per cent, 19.1 per cent, 18.0 per cent, and 21.9 per cent of normal women in the third, fourth, fifth, sixth, and seventh decades, respectively. The incidence of histamine achlorhydria was three to eight times as common in each decade of our series as in Polland's "normal" group.

The relationship of faulty alimentary function to anemia is discussed fully elsewhere, and it must suffice here to mention the evidence which suggests that defective gastric secretion is important in the development of hypochromic microcytic anemia. (1) Whenever extensive gastric operations have been followed by the development of anemia, the anemia has, with few exceptions, been of the hypochromic microcytic type. (2) Complete gastrectomy in animals has also been followed by the development of this type of anemia, especially when pregnancy has been associated. (3) Mettier and Minot¹¹ found that iron is more potent for blood formation when absorbed from an acid than from an alkaline medium within the intestinal tract. (4) The experiments of Dameshek¹² and of Mettier, Kellogg and Rinehart¹³ indicate that a diet rich in organic iron is ineffective in causing a reticulocyte response in cases of idiopathic hypochromic anemia un-

less it has been predigested in hydrochloric acid and pepsin, or in normal gastric juice.

A number of writers have stated that the diets of many patients suffering from chronic hypochromic anemia are lacking in iron-rich foods. Recently, Davidson et al.¹⁴ studied this subject and pointed out that the excess iron intake in the normal diet is only slightly more than is actually needed, especially in women in whom the reproductive and menstrual functions provide a common drain on the hemoglobin stores. Of thirty-five of our patients, regarding whom such data could be obtained, twenty-five (71.4 per cent) took a diet deficient in iron-containing foods. Twelve of these patients lived essentially on carbohydrates, the "tea and toast" diet.

It is our impression, derived from the study of our own cases as well as those recorded in the literature, that in the so-called idiopathic hypochromic anemia, the anemia is the result, in a very large measure at least, of the influence of the three factors discussed; namely, faulty alimentary function, defective diet, and blood loss (including pregnancy and lactation). Achlorhydria alone is not sufficient to cause anemia, as the large number of persons with achlorhydria and no anemia indicates. Although it is conceivable that the diet may be so deficient over a long period of time as to lead to anemia, this actually rarely occurs. When achlorhydria, or a defective diet, or both are present, however, menorrhagia of even moderate degree, pregnancy, particularly several pregnancies in rapid succession, abortion or postpartum hemorrhage, or even normal menstruation may so tax the hemoglobin-building stores of the body that hypochromic microcytic anemia eventually develops. Such an hypothesis explains the sex and age incidence of idiopathic hypochromic anemia as well as its chronicity and lack of spontaneous remissions.

Relapse is common in idiopathic hypochromic anemia. Study of our cases suggests that this is generally due to continuation of the drain on the hemoglobin-building stores. Relapse developed in fourteen of the thirty-one cases with significant gynecologic findings, whereas it occurred in only two of the nine without gynecologic disorders, and even in one of the latter the relapse was associated with the development of menorrhagia for the first time in the patient's experience. In all of the fourteen cases above mentioned, blood loss or pregnancy was associated with the relapse. Relapse developed in one to fifteen months after iron was discontinued.

Of the fourteen patients in whom relapse occurred, spontaneous menopause subsequently developed in one, menopause was produced by radiation in two, and hysterectomy was performed in two. In none of these cases has relapse again developed (eight to thirteen months).

Only in one case has relapse not been associated with continuing

blood loss. This patient's diet is good, and the only abnormality we have discovered is failure to secrete more than a few cubic centimeters of gastric juice or any free hydrochloric acid even after histamine stimulation.

TREATMENT

Intelligent treatment of chronic hypochromic anemia in women necessitates an appreciation of the factors which may cause this type of anemia. Needless to say, it is important, especially in older patients, to rule out demonstrable causes of the anemia, such as malignancy with blood loss. When thorough examination reveals that one is dealing with the so-called "idiopathic" hypochromic anemia, it is of first importance to treat the anemia. The administration of large doses of iron in the form of ferrous sulphate (0.2 gm. t.i.d., p.c.), iron ammonium citrate, 2 gm. t.i.d., p.e.), or reduced iron (1-2 gm. t.i.d., p.c.) is followed in most instances by a rapid restitution of the blood to normal. Only when blood loss was severe, during pregnancy, or when there was some complicating infection, was the response not entirely satisfactory in our cases. It may be noted that relief of the anemia can occur in spite of continued faulty diet and achlorhydria. Persistence in a deficient diet will, however, favor relapse. Its correction will be found more simple as the patient's well-being is regained under iron therapy. The value of liver, kidney, sweetbreads and muscle meat, eggs, such fruits as apricots, peaches, prunes, raisins and apples, and vegetables such as spinach and beet greens, should be stressed.

Unless blood loss is severe, gynecologic therapy may be postponed until the anemia has been entirely relieved and an opportunity has been afforded to observe the gynecologic complaints under more normal conditions. If response is unsatisfactory as the result of continued blood loss, however, gynecologic treatment should be instituted as soon as the patient's general condition permits. The association of relapse with gynecologic disorder, even if there is no other indication, emphasizes the importance of gynecologic attention.

We have been particularly impressed with the great value of suction curettage without anesthesia. If bleeding is in progress, this method will prove a great economy of time in treatment of the anemia. If endometrial hyperplasia or other so-called functional bleeding is present, a single curettage may give relief for several months. This may be repeated as often as necessary until the menopause occurs. If menorrhagia is particularly troublesome, hysterectomy, or castration by radiation may be advisable. If the bleeding is due to myomas of the uterus, operation is the procedure of choice and may be carried out as soon as the patient is in the proper physical condition.

SUMMARY AND CONCLUSIONS

1. A series of 40 patients with hypochromic microcytic anemia of obscure origin (idiopathic hypochromic anemia) has been studied,

particularly from the gynecologic standpoint.

2. Myomas of the uterus were found in 8, endometrial hyperplasia was present in 5, and unexplained menorrhagia was encountered in 14 cases. Twelve patients gave a history of repeated pregnancies, postpartum hemorrhage or abortion. There was evidence of excessive demands for hemoglobin formation in a total of 31 cases (77.5 per cent).

3. Achlorhydria was found in 25 cases and hypochlorhydria in 7 more, making a total of 32 instances (84 per cent of those examined) in which some evidence of faulty alimentary function was found.

- 4. The diet was poor in foods known for their hemoglobin-building properties in 25 patients (71.4 per cent of those regarding whom such information was obtained).
- 5. The etiology of this anemia is discussed, and it is concluded that it is usually the result of the operation of one or all of three factors; namely, faulty alimentary function, defective diet and excessive demands for hemoglobin.

Faulty alimentary function probably impairs absorption of hemoglobin-building materials in the diet; a diet which is low in such foods contributes to the relative deficiency. In most individuals these two factors alone are not great enough to lead to anemia, but moderately increased demands for hemoglobin, and even the requirements of normal menstruation in some women, precipitate the anemia.

- 6. The value of large doses of iron, correction of diet and gynecologic therapy is discussed.
- 7. Relapse is common in this type of anemia and is due in most instances to persistence of increased demands for hemoglobin. Relapse may very often be prevented by checking the excessive requirements.

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A STUDY OF OVARIES FOLLOWING PREOPERATIVE ADMINISTRATION OF AN EXTRACT OF PREGNANCY URINE*

E. C. Hamblen, M.D., and R. A. Ross, M.D., Durham, N.C. (From the Department of Obstetrics and Gynecology, Duke University Hospital)

PREVIOUS reports by one of us (E. C. H.)¹ have been made of studies of ovarian tissue removed at operation from patients who had received preoperative injections of an extract of pregnancy urine which contained the so-called "anterior pituitary luteinizing" factor (APL/PU). One of these reports² detailed the findings in a group of patients with menometrorrhagia in which there was hyperplasia of the endometrium. It is our purpose at this time to present the study of ovaries from a total of 24 patients, who have been placed in three groups: Group I, 9 patients with regular menstrual cycles; Group II, 11 patients with menometrorrhagia ascribed to hyperplasia of the endometrium; and Group III, a miscellaneous group of 4 patients, 1 with delayed puberty and hypogonadism, 1 with inflammatory menometrorrhagia, and 2 with secondary amenorrhea.

CONDITIONS OF THE STUDIES

The ovarian specimens subjected to study have been collected during the last four years. The various members of our staff have aided us in the collection of this material at the operating table. Specimens were subjected to as little trauma as possible in their removal and were fixed promptly in Helly's modification of Zenker's solution. We have excluded from study material from patients with gross or clinical inflammatory processes or benign or malignant tumors of the generative tract.

A gross study of both ovaries was made at the time of laparotomy, and these data were recorded: size of cvaries; presence of and relative number of small cysts; presence of or absence of recent or old corpora lutea; presence of hemorrhage; and any other significant findings. The amount of ovarian tissue available for microscopic study from these twenty-four patients was as follows:

Portion of one ovary	4	cases
Portion of both ovaries	2	cases
One entire ovary	13	cases
Both ovaries	4	cases
Portion of an ovary and an entire ovary	1	case

^{*}Submitted for publication, June 3, 1935.

The expense of these studies was in part defrayed by a grant from the Research Council of Duke University.

When only portions of ovaries were removed, an effort was made to include, if possible, in the removed portion the significant gross findings.

Following fixation and embedding of the ovarian specimens, serial sections cut at 5 micra were made and stained with hemotoxylin and cosin. Thus, all the ovarian tissue removed was available for microscopic study. Significant areas were photographed: a total of nearly 300 microphotographs was taken for aid in reviewing cases and in the tabulation of findings. A large number of these photographs, along with case protocols, charts, etc., formed an exhibit at the Cleveland Session of the American Medical Association in 1934.

Only one commercial preparation of APL/PU was used (antuitrin-S). In most instances, this was reassayed in our own laboratories for potency and where there was disagreement between the stated potency and our assay results, our potency values were used in reporting the dosage. The route of administration was uniformly subcutaneous. The dose at a single injection varied between 100 and 400 R.U. The frequency of dosage varied from one to four times daily. The total dosage ranged from 800 to 8,200 R.U. The duration of injections was from three to thirteen days. The time which elapsed from the last injection until the time of laparotomy varied from one to fourteen days. Injections were given on the second to the thirty-second day of the menstrual cycle. The time that laparotomy was performed varied from the eleventh to the fortieth day of the cycle.

In the selection of material for study the ages of the patients were considered. No senile ovaries were studied. An attempt was made to secure material from the younger patients and the older patients which might allow grouping as to immaturity and maturity. In Group I, the ages varied from twenty-one to forty-four years; in Group III, the ages varied from sixteen to forty-three years; and in Group III, the age variation was from thirteen to thirty-eight years.

GROSS APPEARANCE OF OVARIES

Summary of the gross appearances of the ovaries at laparotomy is omitted, since there were no significant findings which are not included in the tabulation of microscopic findings.

MICROSCOPIC FINDINGS IN OVARIES OF PATIENTS IN THE THREE GROUPS

A. Primordial and Early Follicles.—These were not affected apparently in number or character and corresponded well to the ages of the patients. In Case 14, in which only a very few primordial follicles were seen, only one early follicle was observed in spite of a total administration of 2,400 R.U. of APL/PU with single doses of 200 R.U. twice daily. In Case 7, where a rudimentary and preadolescent ovary was studied, approximately six to seven primordial follicles were seen, but no developing or maturing ones in spite of the total administration of 1,600 R.U. of APL/PU given in single doses of 200 R.U. one to two times daily.

B. Maturing Follicles.—1. Number: The findings of the microscopic study of maturing follicles are given in Table IV. These occurred, as would be expected, more abundantly in the younger patients.

2. Degenerative Changes: A study of the degenerative changes tabulated are given in Table IV. These included cytolysis, theca interna proliferation, and granulosa luteinization. All maturing follicles studied showed some degree of degeneration, usually cytolysis of the granulosa. Proliferation of the theca interna associated with increased vascularization was observed commonly (see Fig. 1). Seventeen cases showed this and in three cases it was quite marked. In two cases there was apparent lutein change in the granulosa. This theca lutein proliferation was marked particularly in the patients in Group II. The only three cases in this group, in which this was not observed, showed no maturing follicles in two instances and only one in another.

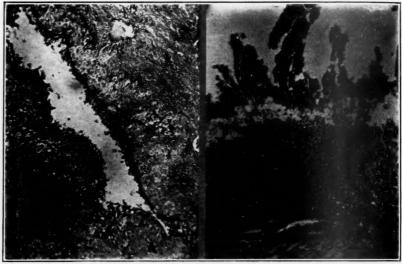


Fig. 1. Fig. 2.

Fig. 1.—Case XIII. Degenerating follicle with cytolysis of granulosa and proliferation of theca lutein cells. $(\times 120)$ Fig. 2.—Case XV. Wall of follicular cyst showing similar changes. $(\times 120)$

3. Hemorrhage: Hemorrhage did not form a striking finding in our studies. In five cases in Groups I and II an occasional follicle showed perifollicular hemorrhage. This occurred in association with increased proliferation of the theca interna and of the thecal vessels. Hemorrhage into the follicles was uncommon and occurred in a single instance in two cases in Group I, in one case in Group III, and in two cases in Group II (see Fig. 3). In all instances except two this hemorrhage was associated with the presence of recent corpora lutea.

C. Follicular Cysts.—1. Number: The relative number of follicular cysts observed in the three groups of patients is shown in Tables I, II, and III, and Table V gives the details of the microscopic findings in these cysts. These cysts occurred more abundantly, as would be expected, in the younger patients with hyperplasia of the endometrium.

2. Degenerative Changes: These include cytolysis, proliferation of the theca interna, especially of the theca lutein cells, and granulosa luteinization. Cytolysis

in the granulosa was observed in varying degrees in all patients in whom follicular cysts were observed. In ten of the twenty-four patients apparent granulosa luteinization was observed. Degenerative changes were observed primarily in the cells furthest removed from the basal layer, whereas in eight cases the cells of the basal layer and near the basal layer showed evidence of proliferation, with frequent mitotic figures. In sixteen of the twenty-four cases proliferation of the theca interna and especially of the theca lutein cells about the cysts was observed (see Fig. 2). All of these cases fell in the younger age group, the oldest patient being thirty-one years of age.

3. Hemorrhage: This did not form a striking finding. Perifollicular hemorrhage in small amounts was observed in four cases and was associated with proliferation of the theca lutein cells and with increased vascularization. Intrafollicular hemorrhage was observed in varying small amounts in seven cases. In only two instances were recent corpora lutea associated.

4. Ova: These in fair state of preservation were observed within the follicular cysts in fourteen of the twenty-four cases. In patients in Group I (those with



Fig. 3.—Case XXIV. Follicle showing perifollicular and intrafollicular hemorrhage. Note the ovum "imprisoned" by lutein cells. ($\times 180$)

regular menses) only one patient failed to show ova in these cysts. This patient was thirty-seven years of age and the portion of ovary examined showed only a few cysts. In Group II only four of the younger patients showed ova in the follicular cysts. The two patients in Group III, in whom ova were not found in the cysts, were a girl of thirteen who had never menstruated and a woman of thirty-eight who had not menstruated in seven months.

D. Corpora Latea and Corpora Albicantia.—Table VI shows the findings in corpora lutea and corpora albicantia. In Group I (patient with regular menstrual periods) recent corpora lutea were found in close agreement with the menstrual cycle. They were not observed in two cases. One of these patients was in the sixteenth day of her cycle and the other in the thirty-third day. In Group II (patients with hyperplasia of the endometrium) no recent corpora lutea occurred in the younger age group (ages 16, 20, 23, 26, 31, 34); they were found in the older age group (ages 32, 32, 40, 42, 43). Recent corpora lutea were not observed in any patients of Group III. In general, it was thought that the age of the hemorrhage and of the lutein cells corresponded well. In eight instances corpora albicantia with recent hemorrhage and, in several instances, with persisting lutein cells were ob-

TABLE I. PATIENTS HAVING REGULAR MENSTRUAL CYCLES

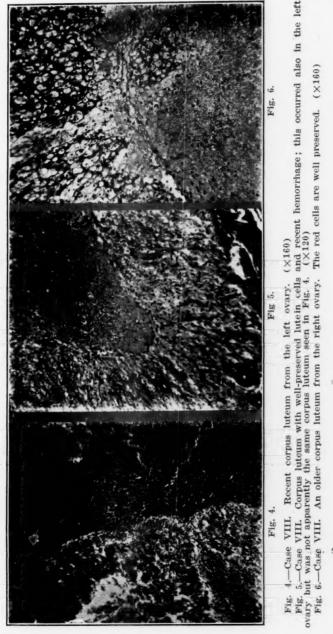
										MICROS	MICROSCOPIO FINDINGS	SDNIGN			
		CONDITION		OF APL/P.U. ADMINISTRATION	ISTRATION	LAPAROT-	,			MATURING FOLLICLES	LICLES		FOLLICLE CYSTS	CYSTS	
CASE	AGE	SINGLE DOSES R.U.	AVERAGE FRE- QUENCY	DAYS OF CYCLE	TOTAL DOSAGE R.U.	OMY (DAY OF CYCLE)		RECENT NUMBER CORPUS PRI- RELA- LUTEUM MORDIAL TIVE FOLLIGLES NUMBER	RELA- TIVE NUMBER	DEGEN- ERATION	HEMOR- RHAGE	RELA- TIVE NUMBER	CHANGES IN WALLS	OVA	HEMOR- RHAGE
24	21	200	2x	7-10	1600	11	+	+++	+++	+++	0	++++	++++	5	3
6	23	200	1x	11-14	1200	16	0	+++	++	++	0	++++	+++	5	1
0.1	27	100	3x	26-32	2100	33a	0	+++	++	+	1	+	+	П	0
22	27	300	2x	16-20	3000	21	p+	+++	+	++	0	+++	++	3	0
1	28	100	3x	7-15	.2700	19	+	++	0	0	0	+	+	1	0
53	32	200	2x	16-17 6-8b	800	17	+ 1	+++	+ +	+++	0	+++	++	ಣ	0
00	36	200	1x	22-28	4000	14	0	++	+++	+++	Н	++++	+++	67	1
21	37	100	2x	2-14	2600	15	+	+	0	0	0	++	++	0	-
5a	44	200	3x	26-31	3000	40	*	+	+++	+++	0	++	++	ಣ	0

*Menses apparently delayed; menstrual history doubted.

bgiven during two previous menstrual cycles. Two other persisting corpora seen with unabsorbed hemorrhage.

⁴Corpus corresponds to cycle; most hemorrhage absorbed (rupture probably occurred before extract began).

served. One case in particular warrants description (Case 8). This patient received APL/PU injections on the sixth to the eighth and the twenty-second to the twenty-eighth day of the two previous menstrual cycles and was operated upon on the four-



teenth day of her third cycle. In addition to the presence of a very recent corpus luteum, two other corpora lutea with persisting lutein cells and fairly recent hemorrhage were observed (see Figs. 4, 5, 6).

DISCUSSION

The effects of the injections of urine of pregnant women have been described in detail by many observers in laboratory animals; the monkey is the only one of these which resembles the human female in having a

TABLE II. PATIENTS HAVING HYPERPLASIA OF THE ENDOMETRIUM

		DETAI	LS OF APL		DMIN-	DIAG- LAP-	OF JES	SEEN	EA
CASE	AGE OF PATIENT	AVERAGE SINGLE DOSE/R.U.	AVERAGE FREQUENCY	NUMBER OF DAYS GIVEN	TOTAL DOSAGE/R.U.	TIME ELAPSED SINCE GOSIS BY D& C AND AROTOMY/DAYS	RELATIVE NUMBER OF PRIMORDIAL FOLLICLES SEEN	RELATIVE NUMBER OF FOLLICULAR CYSTS SI	RECENT CORPORA LUTEA WITH FRESH HEMORRHAGE
10	16	200	1x-4x	6	3200	Same	+++	+++	0
11	20	200-300	2x-4x	9	8200	9	+++	++++	0
13	23	200-300	2x-4x	7	7400	7	++++	++++	0
14†	26	200	2x	6	2400	8	+	1	0
12	31	200	4x	4	3200	7	++	+++	0
16	32	300	2x-3x	4	3000	120	++	+	+
19	32	200-300	3x-4x	7	6600	10	++	+	+
3*	34	100	3x	8	2400	4	+	+++	0
20	40	200	1x-4x	8	3000	13	0	2	+
17	42	200-400	1x-2x-3x	5 .	4400	7	+	+	+
18	43	200-400	1x-2x-3x	6	5400	11	+	++	+

*Menses essentially normal, although dilatation and curettage eight days before laparotomy showed polypoid hyperplasia; menorrhagia developed five months after laparotomy.

†Had had one-third skin erythema dose of deep x-ray to ovaries.

true menstrual cycle. Engle³ notes that "the response of the genital system to anterior lobe principles is the same in no two species of animals which have been investigated." Friedman⁴ has emphasized for the rabbit, and similar deductions have been in other species, that the dosage, route of administration of the given extract, and the condition of the ovary all modify the response obtained. Engle³ further states that "since it appears that the best follicle-stimulating extract tested to date will produce lutein tissue in the rodent with combined injections, the physiologic state of the receptor organ rather than the nature of the active principle accounts for the dual response" (follicle-stimulation and luteinization).

The striking difference in the origin of the corpus luteum in the human being as contrasted with the various laboratory animals and with animals as the sow from which experimental supplies of extracts have been prepared was clearly defined by Robert Meyer⁵ and his concept that the human lutein cell is derived from the granulosa is accepted generally at present. The thecal origin is accepted for the experimental animals.

With these differences in response so apparent in the various laboratory animals a study of human ovarian tissue following APL/PU ad-

TABLE III. PATIENTS WITH OTHER IRREGULARITIES OF MENSES

S	немовинуев	0		t-	0	ಣ
CXS	νλο	0		©1	ಣ	0
FOLLICULAR CYSTS	CHVAGES IN MVIT	0		++++++	+++++	++
FOLI	RELATIVE NUMBER	0		+ + + + +	++++	+
ICLES	немовинуев	0		0	+	0
MATURING FOLLICLES	DEGENERATION	0		+ + + +	+++++	+
TATURE	BELATIVE UUMBER	0		+++	++	+
	BEENORDIVE LOFFICE	+		+ + + +	++	+
	FILERN CORPUS	0		0	0	0
(SINCE INITIAL DOSE)	ro.	•	116	6	9
	TOTAL DOSAGE R.U.	1600	1000	4700	2400	3000
	NUMBER OF DAYS	4	ಣ	10	œ	13
	DVII'X DOSE	1x 2x	1x 9x	3 2 X X	3x	3x
	SINGLE DOSES R.U.	500	500	100-	100	200
	DIAGNOSIS	Delayed menarche; hypogonadism; hypertrophy of clitoris	Metrorrhagia; chronic endometri-	and	Amenorrhea; fourth month puer- perium	Amenorrhea; premenopause
	VGE	13	18		21	38
	CVSE	£-	15		4	9

sion of January, 1933, with bleeding for 19 days; dilatation and curettage after three days of APL/P.U. which had failed to check ^bAdmission October, 1933, with bleeding for 40 days; dilatation and curettage on admission followed by APL/P.U. and laparotomy.

¹Numerals refer to number seen.

TABLE IV. STUDY OF MATURING FOLLICLES

CASE	24	6	¢.1	25	-	23	00	22	10	10	11	100	14	12	16	19	ಣ	50	17	18	1	15	4	9
AGE	21	53	27	27	67 80	35	36	37	77	16	20	67	26	31	35	35	34	40	45	43	13	18	21	90
Cytolytic degeneration	+	++	++	+	0.0	++++	+++	0.3	+ + +	+ 3	+++	+++	+ê	++	0.0	(F)	++	0.0	+ =	++	0.0	++	++	+
Theca interna pro- liferation	++++	+	+	0	0	+	+++	0	++	+	+++	+	0	++	0	+	+	0	+	+-	0	+++++0	++++	+
Granulosa luteiniz- ation	++	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	+	0	0	0	0	0	0	0
Perifollicular hemorrhage	++	0	(1)	0	0	0	+	0	+	0	0	0	0	0	0	0	0	0	0	-0	0	+	0	0
Intrafollicular hemorrhage	+	0	+(1)	0	0	0	(1)	0	0	0	0	0	0	0	0	0	0	0	+	++	0	0	+(1)	0
Individual dosage/R.U. 200	200	200	100	300	100	200	500	100	200	200	200	200	200	200	300	200	100	200	200	200	200	$\frac{100}{200}$	100	200
Doss AP Total dos- age/R.U.	1600	1	200 2100	3000	3000 2700		800 4000 2600 3000 3200 8200 7400 2400 3200 3000 6600 2400 3000 4400 5400 1600 4700 2400 3000	2600	3000	3200	8200	7400	2400	3200	3000	0099	2400	3000	1400	5400	1600	4700	2400	3000
Case		P	Patients		Table I With Regular Menses	I	Mense	92			Patients		With	T	Table II	Table II Hyperplasia of	End	Endometrium	rium		M	Table III Miscellaneous	III	800

TABLE V. STUDY OF FOLLICLE CYSTS

CASE		24	ф.	21	55	7	23	00	21	10	10	11	13	14	12	16	19	က	20	17	18	7	15	4	9
AGE		21	23	27	27	00 61	35	36	37	44	16	20	23	56	31	63	32	34	40	42	43	13	18	21	88
Cytolytic degeneration	ner-	+	1 ‡	‡	1 ‡	+	1	1	+	+	+	‡	‡	0.0	+	(E+	‡	(F)	+3	1 ‡	+	0.0	‡	+	‡
Theca interna proliferation		‡	0	+	0	+	+	+	+	‡	‡	+	‡	0	‡	0	+	0	0	0	‡	0	‡	+	+
Granulosa lutein- ization	n-	‡	+	0	+	0	0	0	+	0	+	0	‡	0	‡	0	0	0	0	+	‡	0	0	0	‡
Perifollicular hemorrhage	em-	‡	0	0	0	0	0	0	0	0	0	0	0	0	+	0	+	0	0	0	0	0	+	0	0
Intrafollicular hemorrhage		‡	+(1)	0	0	0	0	13+	0	0	+(1)	0	‡(9)	0	0	0	0	0	0	0	0	0	‡£	0	‡ €
Mitotic figures seen in granulosa	losa	#	0	0	0	0	+	0	0	‡	0	0	+	0	+	0	0	0	0	0	0	0	+	#	+
Ova in cysts		+(3)	÷(2)	(1)	‡ 🙃	+ (1)	‡ (2)	‡3	0	‡ (4)	0	‡(4)	‡€	0	+(1)	C	‡@	0	0	0	0	0	+ (2)	++ (8)	0
Individual		200	200	100	300	100	200	200	100	200	200	300	300	200	200	300	300	100	200	200	200	200	100	100	200
Dos Art Total dos-		1600 1	2002	100	3000	200 2100 3000 2700		800 4000 2600 3000	2600	3000	3200	8200	3200 8200 7400 2400 3200 3000 6600 2400 3000 4400 5400 1600 4700 2400	2400	3200	3000	0099	2400	3000	4400	5400	1600	4700	2400	3000
Case			Pat	ients	Ta	Table I	I	Table I Patients With Regular Menses	es			Pat	Table II Patients With Hyperplasia of	With	Hyp	Table II	II sia of		Endometrium	rium			Table III Miscellaneous	Table III	18

"No follicle cysts seen; (1), (2) etc., Numerals refer to number seen.

TABLE VI. STUDY OF CORPORA LUTEA AND CORPORA ALBICANTIA

		- P	un	a Lute	Corpu	ж Бесепт		*Oth sh H	T.	Doss Taxti	0
CASE	AGE	Present	Day of cycle	Increase of size	Increase of hemorrhage	Recency of hemorrhage	Recency of lu- tein cells	*Other CL or CA showing recent H or PL	Individual dose/R.U.	Total dos- age/R.U. 1600 1200 2100 3000 2700	Case
24	21	+	11	0	‡	‡	‡	0	200	1600	
6	67	0	16	X	X	×	X	CA 1 H	200	1200	P
61	27	0	66	X	X	×	X	0	100	2100	atient
61	27	+	21	0	0	+	‡	0	300	3000	T a Will
1	01 00	+	19	+	+	‡	‡	G H	100	2700	Table I Patients With Regular Menses
233	35	+	17	0	0	‡	‡	0	200		I
00	36	+	14	0	0	‡	‡	CH CH	PL 200	4000	Mens
61	37	+	15	+	+	‡	‡	0	100	2600	ses
50	77	+	40	0	C	+	+	CA 1 PL	200	800 4000 2600 3000	
10	16	0	X	X	X	×	X	CA 1 H	200	3200	
1	20	0	X	X	X	X	×	0	200	8200	Pati
13	233	0	X	X	×	X	X	CA 1 H	200	7400	ents
14	56	0	X	X	X	X	X	0	500	2400	Table II Patients With Hyperplasia
12	31	0	X	×	X	×	X	0	200	3200	T
16	65	+	×	0	+	‡	+++++	0	300	3000	Table II
19	35	+	X	+	+	#	‡	0	300	3200 8200 7400 2400 3200 3000 6600 2400 3000 4400 5400 1600 4700 2400	II sia of
ಣ	34	0	60	×	×	×	×	0	100	2400	
20	40	1+	X	‡	‡	#	‡	CA 1 H	200	3000	Endometrium
17	42	1+	X	+	+	‡	+	E P L	200	1400	ium
18	65	+	1	‡	‡	‡	‡	0	200	2400	
1-	13	0	X	×	X	X	×	C	200	0091	M
15	18	0	×	X	×	X	×	0	100	4700[2	Table III Miscellaneous
4	21	0	X	×	X	×	×	0	100	400	III
9	80	0	X	X	X	×	X	0	200	3000	

ministration seemed justified. The rather general use clinically of certain commercial preparations of APL/PU and the equivocal results reported by many seemed to urge a careful consideration of the possible method of action, if any, of such preparations. With the various hemorrhagic and lutein changes seen in the ovaries of rodents in mind, one was led to question the possibility of serious damage from such administrations to the human ovary, particularly in the immature patients.

We are in thorough agreement with Pratt⁶ when he notes: "A true evaluation of the normal ovary is difficult to attain, for the literature concerning the normal ovary is inadequate for obvious reasons. The best material is obtained at operation, and naturally most operations are performed on account of preexisting pathologic states. My observation is that a normal ovary does not frequently show evidence of hemorrhage, but that even the gentlest manipulations exerted to bring the organ into clear view readily produce slight hemorrhages, a fact which is easily explained when the delicacy of the newly forming capillaries is considered. The traumatization during removal accounts for many of the recent hemorrhages seen in laboratory specimens." Our interpretation of our findings must be made in the light of our meager concepts of the normal human ovary, gained chiefly from its appearance at operation and from the microscopic study of specimens of ovary which are available from surgical pathologic and autopsy specimens.

The assumption seems warranted that primordial follicles and early developing follicles are not affected by these injections. This is illustrated apparently by Cases 7 and 14, in which there were observed primordial follicles but no maturing ones. Were the action of the APL/PU on these, one should expect to find some evidence of development or maturation.

Pratt⁷ citing recent work on ovogenesis in the adult, especially that of Evans and Swezy⁵ and the unpublished work of Edgar Allen (confirming ovogenesis in the human being) calls attention to "the careful consideration of the possible influences on continued new formation of ova in the adult ovary" that may be exerted by these extracts. It is difficult to get sections showing good germinal epithelium, but with modifications of technic, our sections may allow a review with consideration of these problems.

The degenerative changes observed in these maturing follicles have formed an interesting part of our studies. These changes are in all essentials those expected in the life cycle of the graaffian follicle, for as Engle³ notes: "Save for the granulosa cells which undergo lysis in atretic follicles, there is no other fate for granulosa cells than that of transformation into lutein tissue." The most striking of the degenerative changes observed is an apparent increased activity of the theca interna, and especially of the theca lutein cells with increased peri-

follicular vascularization. This is quite marked about the majority of the maturing follicles and follicular cysts. When one studies these follicles and cysts, one appreciates the similarity of these to the changes seen in the ovaries of rodents. The theca lutein cells have proliferated as in the rodent but without formation of true lutein cells in the human being but rather of para-lutein cells. Such stimulation in the rodent produces true lutein cells. Hemorrhage into these follicles and cysts does not occur in our sections except in a few instances. Where it does occur, it may well be explained at least in part by surgical trauma and thecal vascularization.

It is interesting to speculate whether these proliferating theca lutein cells secrete progestin. Since the presence of progestin has been demonstrated in small amounts in association with corpora lutea in the human being, 6, 6 an assay for progestin content of ovaries which show no corpora lutea after APL/PU administration would be of value in solving this problem.

We were impressed also by the changes in the granulosa of the follicular cysts and by the relatively large number of contained ova in fair state of preservation. The observed mitotic figures in the granulosa cells and the number of these cells seemed to indicate either stimulation of developing follicles resulting in the recent formation of those cysts or the reactivation of the lining cells of cysts already formed. The former assumption seems more likely to us, as it explains also the good preservation of the ova.

There were five instances in which we may be forced to assume ovulation followed the administration of APL/PU if we agree with the generally accepted view as to the etiology of hyperplasia of the endometrium as emphasized by Burch and his coworkers.¹⁰ These occurred in patients with hyperplasia of the endometrium whose ages were 32, 32, 40, 42, 43 years and in whose ovaries recent corpora lutea were found. It would seem reasonable to assume also that premenstrual endometrium and normal menses might have resulted. This is in accord with the clinical observation of some of those who have used APL/PU in the treatment of this condition; that it is much more effective in controlling the excessive menses in the older age group of patients than in the younger patients. It would seem evident that any beneficial result obtained in the younger patients could not be inferred as coming from the production of a true corpus luteum, induction of ovulation or correction of the basic ovarian or endometrial pathology. The fact that corpora lutea were found in general as expected from the menstrual cycle in women with regular menses, were not found in women with amenorrhea or in the younger patients with endometrial hyperplasia seems to indicate that ovulation, as a rule, is not induced by these injections.

One may question if the cause of excessive bleeding, attributed to hyperplasia of the endometrium, is the same in the younger and in the older patients. If one is sure of the sameness of the etiology, the explanation of the consistent difference in response must be made on the basis of the inherent difference in the ability of the younger and the older ovaries to respond to the same stimulus.

The study of corpora albicantia, some of which show recent hemorrhage with persisting lutein cells, and of the corpora lutea in Case 8, in particular, leads us to speculate that this extract may tend to promote persistence of lutein cells in preformed corpora lutea. Such a function would be compatible with the abundance of the APL factor in pregnancy and might point to its physiologic purpose of preserving the corpus luteum of pregnancy.

In general the changes which may be attributed to administration of the extract are primarily degenerative. One would not expect changes in these ovaries qualitatively much different from those observed as a result of the ordinary degenerative changes which are a part of ovarian physiology or would one expect these quantitatively much different from those seen in the ovaries in pregnancy which are subjected to the same principle in probably much higher concentration. The primordial and very early follicles show no definite changes. Stimulation to maturation of developing follicles may occur with proliferation of the theca interna, especially of the theca lutein cells, with increased vascularization. The follicles may develop rapidly, perhaps, into follicular cysts, with still active granulosa and surrounded by proliferated theca interna, in which theca lutein cells are very prominent (para-lutein cysts). Ovulation would not be favored in such cases. Preformed lutein cells are aided probably by increased vascularity to persist. Such changes could be of a temporary nature and rapid regression follow cessation of the extract administration. New developing follicles could result from the primordial follicles which are not damaged apparently. One fails to see in this type of action any changes which are desired in the normal menstrual cycle, but one can well understand their possible rôle in the pregnant woman.

These findings differ from those of Mandelstamm and Tschaikowsky¹¹ and of Geist.¹² Their findings were summarized in a previous report by one of us.²

Mandelstamm and Tschaikowsky reported on the effects of daily subcutaneous injections of prolan varying from 100 to 200 M.U. with total doses from 400 to 1,100 M.U. The ten women studied had normal menstrual cycles and were operated upon on account of fibromyomas, carcinomas of the cervix, or unilateral ovarian cysts. Six of the patients were between thirty and forty years of age, two between forty and forty-five years, and two between twenty and thirty years. The interval be-

tween the last injection and operation as well as the time in the menstrual cycle varied. They noted degenerative changes in the maturing and mature follicles which included defective ova and disintegrative and degenerative changes in the granulosa. There were cystic follicles, numerous corpora lutea and hemorrhages into the follicular apparatus. They felt that these changes were sufficient to produce a temporary sterility.

Geist has reported a study of the effect of injections of antuitrin-S on the mature human ovary from patients ranging in age from thirty-three to forty-eight years; the majority of those patients was operated upon because of uncomplicated fibroids. The total subcutaneous dosage varied from 600 to 2,200 R.U.; total daily dosage was in some instances 600 R.U.; period of administration was from thirty-six to one hundred hours. He noted occasional gross hemorrhages in the ovaries suggestive of a positive pregnancy test in the rodent. He was impressed also with the absence of what might be called follicle stimulation; the number of cystic follicles was increased apparently; theca lutein cells were thought to be increased. He thought that the intensity of the responses seen in the ovaries was directly proportional to the amount of injected hormone.

SUMMARY

- 1. A study of ovarian tissue from twenty-four patients following preoperative administration of APL/PU is detailed.
- 2. Primordial follicles are not affected apparently by such administrations.
- 3. Degenerative changes apparently resulting from folliele stimulation are described.
- 4. The end-result of these changes appears in many instances to be follicular cysts, with active granulosa and fairly well preserved ova, and surrounded by a proliferated theca interna with prominent theca lutein cells (theca-lutein cysts) and with increased thecal vascularization.
- 5. Some evidence is adduced that persistency of preformed corpora lutea may result from such administrations.
- 6. Attention is called to the apparent difference in response in the ovaries of the younger and older patients with hyperplasia of the endometrium.
- 7. In general, it is believed that ovulation is not induced by such administrations.
- 8. The possible action of these extracts in many respects is more typical of the gestational cycle than the menstrual cycle.
- 9. One should probably expect no material qualitative or quantitative difference in the changes in these ovaries from those of ovaries in pregnancy.

10. One is led to question seriously the clinical value of such action on the ovaries of the nonpregnant woman.

11. Such changes as described are probably temporary in nature and it may be that no permanent damage results.

We have been furnished generous supplies of antuitrin-S for these studies by Dr. E. A. Sharp, of Parke, Davis and Company, to whom we are grateful. We wish to express to Dr. J. P. Pratt our appreciation for his many helpful suggestions in carrying out these studies. The close cooperation of the members of our department and of the Department of Pathology has been of paramount importance in the collection of this material for study. Dr. Wiley D. Forbus, head of the Department of Pathology, has aided us materially by supplying assistants for much of the technical work. The faithful and careful work of our research technician, Miss Margaret Baptist, has been invaluable.

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Because ketogenic diet requires rigid supervision of patient and diet, and is not pleasant, or suitable in the home, an attempt was made to find a keto- or hydroxyacid which would be nontoxic and excreted unchanged in the urine.

B. coli has been the test organism against the following acids: B-hydroxybutyrie, B-hydroxypropionic, laevulinic, lactic, pyruvic, benzoic, hippuric, benzoylaeetic, B-phenyl-B-hydroxypropionic, and mandelic. B-hydroxypropionic, laevulinic, benzoylaeetic, and mandelic offered promise. The first three were eliminated since they were either oxidized in the body or did not produce clinical results. Mandelic acid was nontoxic, was excreted unchanged, and had bacteriostatic action.

An ounce mixture containing 3 gm. of mandelic acid, 1.6 gm. sodium bicarbonate flavored with lemon was given four times daily while eight cachets containing 1 gm. of ammonium chloride were taken daily.

Twelve patients (6 pregnant) have received this treatment. Subjectively and objectively the patients improved rapidly. It is necessary to control the urinary pH by estimation with methyl red. Buzzing in the ears and temporary deafness occurred in two or three patients.

Mandelic acid appears to be effective in cases of urinary infection unassociated with urinary obstruction.

H. CLOSE HESSELTINE.

THE INFLUENCE OF COLLAPSE THERAPY IN THE TREAT. MENT OF PULMONARY TUBERCULOSIS ON MENSTRUAL PHYSIOLOGY

EDWIN M. JAMESON, M.D., SARANAC LAKE, N. Y.

THE increased use of procedures designed to collapse the affected lung in pulmonary tuberculosis makes a knowledge of the influence such operations have upon the pathologicophysiology of other systems of the body desirable. To the phthisiologist and the thoracic surgeon, whose attention is focused upon the effect the artificial pneumothorax or thoracoplasty has upon the tuberculous lesion per se, such by-products in the female genital system may appear incidental and of but little importance. To the patient herself, however, and to the physician who is called into consultation and who is not familiar with the alterations that may be expected, they frequently present annoying problems.

Tuberculosis in any form can no longer be regarded as a disease of any one organ or system but must be recognized as a general disturbance of the economy of the entire organism. It is true that the various forms of the disease react with varying degrees of intensity upon the other systems and that in the acute forms of tuberculosis the reaction is likely to be more severe and more pronounced than in the more chronic types. As examples, one may cite bone and joint tuberculosis, which is comparatively chronic and benign and which has but little effect on the pathologicophysiology of the nervous, digestive, and genital systems, in contrast with the usual forms of pulmonary tuberculosis in which such side-effects are frequently prominent and may have a profound influence on the ultimate prognosis.

In some instances the alterations in the menses experienced by tuberculous women are transitory and will disappear with improvement in the pulmonary condition. Such a prognosis has been recognized since physicians began to interest themselves in the problems of menstruation, and its accuracy has, no doubt, been attested on innumerable occasions. To one who has had the opportunity of following a large number of tuberculous women through the months of their sanatorium residence and of observing them at intervals after the pulmonary disease has become arrested and even cured, however, the large number who continue to have menses which differ from the individual's normal habit that was established before the onset of tuberculosis is striking.

It must be emphasized that all such alterations in the menses of tuberculous women are not for the worse. We have observed, for

example, a well-defined group in whom menstruation became more nearly "normal" after the onset of tuberculosis; in some instances patients heretofore irregular began to menstruate at twenty-eight-day intervals; in others an annoying and persistent leucorrhea, frequently looked upon as evidence of a "run-down condition" or "weakness," disappeared. In an analysis of such symptoms previously reported,1 about 10 per cent were found to have less dysmenorrhea since the onset of tuberculosis and 12 per cent more. In the face of such evidence it would appear unwise and rather savor of post hoc reasoning to dismiss the question of alterations in female genital physiology in pulmonary tuberculosis by attributing all of them to a hypothetical "toxemia" without giving due consideration to the possibility of an independent endocrine dystrophic basis for the changes presented.

In previous publications^{1, 2} we have presented studies on the pathologicophysiology of the female genital apparatus in tuberculous women who have been on the dietetico-hygienic medical regime commonly employed in pulmonary tuberculosis. Comparisons were drawn between the menstrual functions before and after the onset of tuberculosis, and an attempt was made to indicate the changes qualitatively and quantitatively. In a survey of the influence of artificial pneumothorax therapy on menstruation, it was found that changes were produced in many instances and that only a few of the group reported improvements as described by Caussimon.3 Specifically, it was found that approximately one-fourth of the patients subjected to pneumothorax therapy had had changes in menstruation consisting of increased irregularity, more dysmenorrhea, amenorrhea of longer or shorter duration, and alterations in the amount of flow and length of the intermenstrual interval. The institution of artificial pneumothorax therapy may also result in an increased premenstrual fever in some instances. In a group of eleven patients one had less flow after beginning collapse therapy, one had the intermenstrual period increased from twenty-eight to thirty-five days, and in two others, the interval was decreased below the normal of twenty-eight days. One patient returned to a twenty-eight-day schedule.

The present study was made for the purpose of elucidating the influence of thoracoplasty on the menstrual function. Because the physician who has occasion to see tuberculous women is not infrequently confronted with patients in whom the menses are accompanied by functional disturbances of such severity that they undermine the patient's resistance to a point at which she can no longer make progress in the healing of her tuberculous lesion during the intermenstrual weeks, the question of prognosis without the necessity of producing an artificial menopause by radiation often arises. In other words, will a successful thoracoplasty in these women, who are

usually but not always in the group with far-advanced pulmonary tuberculosis, result in an alleviation of the disabling menstrual symptoms or will it increase them? If the latter, what does the induction of an artificial menopause offer not only to the prognosis of the thoracoplasty itself but to the ultimate general condition of the patient as well?

The following cases may be cited as illustrative of the type:

Case 1.—Patient, aged twenty-six, married, white, was seen on Oct. 21, 1929 for a complaint of pain in the right lower quadrant. She had had pulmonary tuberculosis for a number of years for which artificial pneumothorax had been administered with satisfactory immediate results. After the lung had been allowed to reexpand there was a reactivation of the tuberculosis and the patient was now undergoing her second regime of treatment in Saranac Lake. For some time she had complained of pain in the right lower quadrant which began about four days before the onset of alternate menstruations. The pain was not considered severe until two months before the first consultation; at that time it was accompanied by a fever of 101° F. The last menstruation was unaccompanied by the pain and the temperature was only 99° F. The pain recurred, however, with the present period and has persisted even though the flow stopped about a week before she was seen. There was no change in the type, amount, or duration of the flow. Menstruation was accompanied by a sensation of weight in the pelvis. Menstrual history, 17 x 28 x 3, dysmenorrhea as noted above, moderate amount of flow, no metrorrhagia. Para 0, miscarriages none. The late puberty was attributed to anemia and streptococcic throat infections present during that time. There were no gastrointestinal symptoms although a barium meal demonstrated irregularities in the region of the ileocecal valve which were thought to be caused by adhesions. There were no urinary tract symptoms. Previous medical history included an attack of acute appendicitis at the age of fifteen, for which no operation had been performed, and several attacks of quinsy between the ages of fourteen and seventeen years. Physical examination at the first visit showed a poorly developed and nourished adult white female who appeared acutely ill. The gallbladder and kidney regions were negative. There was an indefinite, evasive and movable mass in the right lower quadrant which was not tender and too high up to be palpated vaginally. The external genitalia and vagina were healthy. The external os was small and closed. The uterus was small, firm, smooth, normally A.F. and A.V. but seemed to be pulled to the right. The left tube and ovary were negative. The right appendage could not be outlined because of tenderness but no masses were palpable. Hemorrhoids were present. Because of the patient's poor general condition it was decided to treat her symptomatically for the present.

She was seen again in April, 1930 at which time her general condition was noted to be considerably worse. She gave a history of rises in temperature to 99.4° to 101° F. beginning two weeks before the onset of each menstruation. Until two or three months ago the fever fell to normal two days before the appearance of the flow but it now continues through the period. For the past four months it has reached 101.6° F. with each menstruation and during the present one attained 103° F. She complained of occasional right lower quadrant pain which bears no definite relation to the menses as a rule but was more severe during the period just completed. The present menstruation was also accompanied by pain in the vagina. The periods are now very scant, last only a day and a half, and are accompanied by a sensation of weight in the pelvis and pain across the lower lumbar region. The physical findings were similar to those noted on the first consultation.

Because of the severity of the menstrual symptoms it was decided to employ roentgen ray therapy to induce an artificial menopause. Such treatments were started six weeks later and a total of 6 given during the succeeding five months. There was marked improvement in the entire picture and in November, 1930 the patient was subjected to the first two stages of the thoracoplasty operation which she underwent satisfactorily. Three months' amenorrhea supervened which were attributed to the x-ray treatments but could have been caused by the thoracoplasty per se. When menstruation was resumed in February, 1931 it was accompanied by a comenstrual fever of 100.4° F. and lasted eight days. In December, 1931 increased pulmonary symptoms began to appear with the menses and persisted about ten days. In January, 1932 a third stage thoracoplasty was carried out. A note in April, 1932 states that there were increased cough and expectoration with the menses and a premenstrual fever of 99° to 99.6° F. In August, 1932 a note was made that there was no increase in pulmonary symptoms accompanying the periods although the patient was not doing well. In January, 1933 there was an attack of influenza (?) with accompanying hemoptysis at the time of the menstruation. In February, 1935 a reexamination of the patient showed her to be apparently much improved and she stated that she felt better than at any time since the thoracoplasty had been done. An intercurrent attack of pneumonia terminated the picture in May, 1935 after the patient had returned to her home.

CASE 2.—Patient aged thirty-two, married, white, was seen in December, 1934, for exaggeration of her pulmonary symptoms with each menstruation. She had been under treatment for pulmonary tuberculosis for three and one-half years and at the present time was classified as a far-advanced case with cavitation in the left lung. The gastrointestinal tract was normal. The patient gave a history of increase in her chest symptoms with each menstruation since the onset of tuberculosis. These symptoms were described as being similar to those felt when one has a "cold" in the chest and were accompanied by increased expectoration and, during the last period, with a temperature of 99 to 99.4° F., which began four or five days after the flow started. She stated that she lost 1 to 11/2 pounds with each menstruation. Menstrual history, $11 \times 28 \times 5$ -8, no pain, profuse flow for several years after puberty, no metrorrhagia or leucorrhea. In 1920, following an attack of influenza, the menses became irregular and a period of two to three months' amenorrhea occurred. Five roentgen ray treatments at intervals of two weeks were administered during the past summer and were followed by more regular intervals between the menses. The details of these treatments were not available. The patient felt that the sensations of pulmonary congestion during the menses were improved while the x-ray treatments were being given and no fever accompanied the periods during that time. The congestion and fever had, however, been markedly worse during the past two menstruations. Since the x-ray treatments there has been a tingling sensation in both ovarian regions. The breasts swell and are very sore at the time of the menses; these symptoms usually begin five to six days before the flow appears. Married four years, no pregnancies.

Physical examination showed a well-nourished and developed white female in whom the abdominal examination was essentially negative. The introitus was marital, the cervix long and conical, and a moderate periorificial erosion was present. The uterus was small, in normal position, and the appendages were negative.

The patient was a candidate for thoracoplasty and the question presented was whether or not some line of treatment for the menstrual difficulties should be undertaken before the operation was carried out or whether it was likely that they would disappear following the procedure. From an analogy with the experience derived from the artificial pneumothorax studies, it was deemed unlikely that the thoracoplasty would result in improvements in the menstrual picture. However, as

the patient was then considered to be in good condition for the operation, it was thought unwise to delay it any further for a trial of glandular or roentgen ray therapy and take the risk of an exacerbation in the pulmonary condition which would delay operation. It was felt that if the menstrual symptoms persisted after thoracoplasty they could then be treated.

A two-stage thoracoplasty was successfully performed in February, 1935. Uterine bleeding occurred twice during the month and was present at the time of both operations. The first menstruation after operation was normal but the second, which was ten days late, was accompanied by the onset of a pleurisy with effusion and was quite profuse. The last period appeared after a twenty-seven-day interval, was scant and painless, and was accompanied by nausea. Sufficient time, of course, has not elapsed since the operation to determine its ultimate effect on the menses but, if one may judge from the data detailed below, it is improbable that it will result in alleviation.

Such instances as these would seem to make a study of the influence of collapse therapy on menstruation highly desirable not only for diagnostic purposes but also in order that an intelligent prognosis may be made. Accordingly a group of seventy-four women upon whom thoracoplasty had been carried out at least six months before and in whom the results were considered good were questioned. Approximately half of these patients were operated upon in Saranac Lake and the remainder were secured through the cooperation of Dr. Margaret Cameron of the Royal Victoria Hospital in Montreal, Canada. As data on all the questions were not obtained in every case, discrepancies in the totals may be noted.

Of this number there were eleven patients whose menses were irregular before operation. Ten of these have since resumed a regular menstrual schedule and one has remained irregular. Of fifty-seven patients who were regular before operation, five (8.7 per cent) have become irregular. One patient who was amenorrheic before thoracoplasty resumed regular menstruation afterward.

The average number of days of flow showed no appreciable difference before and after thoracoplasty and striking individual changes were not noted. Seventy-four and three-tenths per cent showed no change; 5.5 per cent had a slight increase and 15.2 per cent reported a decrease in the number of days of flow. The patient who was amenorrheic before operation resumed menstruation after thoracoplasty with five to seven days of flow and a second patient who had menstruated regularly before operation with four or five days of flow underwent her menopause soon after the lung had been surgically collapsed (she was forty-five years of age).

In seven instances (9.4 per cent) thoracoplasty was followed by amenorrhea for one to six months with an average of four months for the group. In several additional instances the menstruation that followed the operation was delayed.

Approximately 80 per cent of the patients experienced no change in the amount of flow after operation; in 13.4 per cent it decreased appreciably and in 7.4 per cent there was an increase. In 65.6 per cent the amount of flow was considered normal before operation and in 64.2 afterward. Six patients who had a normal amount of flow before operation considered it abnormal afterward.

The incidence of dysmenorrhea remained unchanged after thoracoplasty (43.6 per cent). Of the 28 patients in the group who had menstrual pain before operation, 2 have had none since, 11 have had less, 2 more, and 13 have had no change. Of the 45 patients who had no dysmenorrhea before thoracoplasty, four (9.1 per cent) have developed an appreciable amount since operation. In several instances (7 per cent

of the group) pain described as severe and incapacitating before operation was ameliorated afterward. In no case did a slight dysmenorrhea become severe after operation.

Miscellaneous menstrual symptoms apart from dysmenorrhea were prominent. Three patients who were nauseated at the time of the menses before operation were relieved as a result of the procedure; one patient developed such nausea after thoracoplasty. Four patients complained of nervous symptoms such as vertigo and headaches before operation; since operation, this number has been doubled. Six of this latter group had no such symptoms before operation; in two instances in which the symptoms were present before operation they have since disappeared and in two instances the symptoms were unaffected by the procedure. One patient developed extreme weakness during menstruation after thoracoplasty. One patient had hemoptysis with menstruation before operation and one patient has developed such hemorrhages since operation (this patient also has profuse hemorrhages from the gums at the time of the menses although no cause is apparent).

Menstruation has been accompanied by pulmonary symptoms described as "shortness of breath," "sense of fullness in the chest on the operated side," "cough," and "increased expectoration" (negative sputum) in 7 patients (about 10 per cent) since operation. One patient who had such symptoms before operation has been relieved since.

Leucorrhea has developed in 15.2 per cent of the patients since operation. In 6.7 per cent of those who had a vaginal discharge before operation, there has been none since. In 5 per cent of the group leucorrhea appeared immediately following operation, lasted a greater or less time, and then cleared up spontaneously.

The data on the influence of thoracoplasty on premenstrual fever are incomplete and probably inaccurate because so many of the patients have not taken their temperatures regularly since returning to their homes. However, it is known that two women (3 per cent) who had no such fever before operation have developed it since. In the majority of patients in whom a premenstrual fever occurred before thoracoplasty, the procedure resulted in no change in its range or duration. A few patients noticed that whereas the premenstrual fever had been accompanied by extreme discomfort before operation, they now suffered no inconvenience or incapacity from it.

Of the six patients who had a comenstrual elevation of temperature before operation (9.3 per cent), five have shown no such rise since thoracoplasty. Three patients who had no menstrual fever before operation have developed it since and all are in poor condition. This observation would tend to bear out a previous statement that comenstrual elevations of temperature in pulmonary tuberculosis are evidence of a bad prognosis.¹

Postmenstrual fever which was present in five cases (7.8 per cent) before operation has since disappeared; in two instances such fever present before operation has continued since. Thus in five out of seven instances in which there was a postmenstrual fever the condition has been relieved as a result of the operation.

In a smaller group of thirteen women in whom the results of the thoracoplasty were considered poor or incomplete, the menstrual changes were somewhat less marked but the figures make an interesting comparison with the first group. Of this series two who were irregular before operation showed no change afterward. One patient who had been amenorrheic for two years before operation, during which time she had gained considerable weight, and in whom the procedure resulted in an 80 per cent collapse of the affected lung, began to menstruate every twenty-eight to thirty-one days after the thoracoplasty had been carried out. Of the ten patients in the group who were regular before operation two have since become irregular and one (aged forty-five years) has had her menopause. The number of days of flow decreased in two patients and five patients (exclusive of the one who passed through the

menopause postoperatively) reported less menstrual flow. With the exception of the patient who had been amenorrheic before operation, none of the group showed increased flow. Dysmenorrhea appeared for the first time in one patient after operation, and in three instances in which menstrual pain had been present before thoracoplasty, there was increased discomfort afterward. Seven of the eleven patients who answered this question suffered from dysmenorrhea. Leucorrhea appeared postoperatively in three patients in this group and decreased in two.

SUMMARY

1. The increased use of surgical procedures to collapse the affected lung in pulmonary tuberculosis makes an appreciation of the "by-products" of such operations desirable.

2. Alterations in the pathologicophysiology of the genital tract in women with pulmonary tuberculosis have long been recognized. For diagnostic and prognostic purposes, a study of the influence of the various therapeutic measures now in use is indicated.

3. In the present study on seventy-four cases it has been shown that thoracoplasty results in definite changes in the menstrual function and that, while some of these changes are obviously for the better, others would suggest still further derangement of the genital physiology.

4. The improvements noted can be explained in some instances by the general improvement in the patient's physical condition; the untoward results cannot always be attributed to an increase in the tuberculous lesion or to a further deterioration in the patient's health.

5. It would seem that the usual explanation of a "toxemia" of tuberculosis as the cause of abnormal menstruation in tuberculous women is inadequate and that the problem should be approached from the same angle and with the same broad viewpoint that obtains in the investigation of endocrine dystrophies in nontuberculous women.

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At the Kiew Woman's Clinic the quartz lamp was found often to produce regressive changes in condylomas up to disappearance. The lamp through bactericidal effect overcomes the inflammation which is responsible for the development of the condylomas. This treatment also diminishes the pain connected with these lesions.

J. P. GREENHILL.

VACCINATION DURING PREGNANCY AS A PROPHYLAXIS AGAINST PUERPERAL INFECTIONS

A PRELIMINARY REPORT

J. BERNARD BERNSTINE, M.D., F.A.C.S., AND RALPH EDWARD OTTEN, M.D., PHILADELPHIA, PA.

(From the Department of Obstetrics, Jefferson Medical College and Department of Obstetrics and Laboratory of Bacteriology, Philadelphia General Hospital)

THE problem of immunity to puerperal sepsis has attracted the attention of clinicians and biologists ever since the bacterial origin of infection has been recognized. In 1923 and 1925 Dick et al. inaugurated a cutaneous test for the toxin of scarlet fever. Later, this test was extended to the field of obstetrics and patients were examined for susceptibility by the Dick method. These investigations added much to the knowledge of immunity to certain strains of the streptococcus and have emphasized the importance of the natural resistant agents of the body in combating and eradicating infection.

The problem in puerperal sepsis, however, goes beyond the question of streptococcic infection alone. While the most severe of the blood infections are generally due to hemolytic strains, many other morbid lesions are produced by bacilli of the colon group and various other cocci. With these facts in mind the authors have undertaken to culture the types of organisms commonly found in puerperal infection, test their effect upon laboratory animals, and by means of a vaccine made from the cultures, endeavor to elevate the immunity of the pregnant woman to puerperal infection in general.

The content of this paper has to do with the technic of preparation, the experimental trials in mice, and the results obtained by the use of the vaccine in fifty-one pregnant women. While the number of cases is at present limited, many were of such a nature as to make the results appear favorable and justify in our minds the publishing of the report.

Our first problem was to study carefully the bacteriology of the birth canal, especially the cervix and endocervix of pregnant women. The bacterial strains employed in the vaccine used in our study were obtained from the patients (pregnant women) attending the antenatal clinic of the Philadelphia General Hospital. The cases studied were picked at random and not selected, the only requirement being that the patient employed should have had no sexual intercourse for at least twenty-four hours preceding the taking of the cultures, nor to have taken a vaginal douche.

The patient thus employed was placed in the dorsal position, and a dry, sterile bivalve vaginal speculum was introduced into the vagina. The other hand, still being uncontaminated, was employed in obtaining the cultures. These were obtained from the cervix with a sterile cotton swab while the assistant immediately placed this specimen in a sterile tube containing blood agar, solidified, to prevent drying of the specimen. The second specimen was taken from the endocervix, and treated likewise. All specimens were taken to the laboratory and subcultured within thirty minutes from the time they were obtained.

CULTURAL MEDIA AND METHODS

For the purpose of isolation and identification of organisms, we employed 5 per cent defibrinated horse blood agar plates and slants, beef infusion broth, pH 7.6 and plain 2.5 per cent infusion agar plates and slants. In the case of gram-negative bacilli, their identification was made certain by their carbohydrate fermentation reactions.

Each of the two specimens was streaked to each of two blood agar plates and then the swabs were placed separately in test tubes containing 5 c.c. of beef infusion broth. One of the blood agar plates from each specimen was incubated under partial oxygen tension, the two remaining plate cultures being kept at normal aerobiosis. The reduced oxygen tension was obtained by placing the cultures in Novy jars and partially evacuating the air by means of a Cenco-Hyvac pump. All cultures were then incubated for twenty-four hours at 37.5° C., when they were examined for growth, grossly and microscopically. The broth cultures were subcultured to blood agar plates and incubated under conditions of both normal and partial oxygen tension for twenty-four hours or longer. No culture was considered negative for growth until after an incubation period of at least seventy-two hours. No direct smears from patients were made, since we were interested only in bacterial growth. However, routine smear preparations are studied on all patients in this clinic for evidence of neisserian infection.

In the series of twenty-five cases studied we failed to recover any organisms from the cultures grown under partial oxygen tension which we did not obtain in cultures grown at normal oxygen tension. The gonococcus was conspicuous by its absence in all cultures.

The strains to be incorporated later in a vaccine were placed in pure culture on suitable media and stored at a temperature of 6° C. as soon as their isolation and identification were made.

The complete bacterial flora of the series studied is shown in Table I. We have not listed the cultural results from the cervix and endocervix separately, because we found only a slight and insignificant variation in the bacterial flora from the two sources.

PREPARATION OF THE VACCINE

The majority of the various strains of organisms incorporated in the vaccine were pathogenic for mice. Only strains which grew smoothly in broth and produced smooth colonies on solid media were employed. All of these latter strains were grown by repeated transfer in broth for four successive days and then the growth from an eighteen-hour culture was collected in sterile physiologic saline, washed once with normal saline and standardized to 2 billion per c.c. by the turbidity method, using as standards of comparison suspensions of staphylococci in gelatin of a 2 billion per

FECALIS ALKAL.																		+								-	40% 40%
B. PROTEUS			+																							1	46
YEASTS	+												+			+							+			4	16
B. SUBT.	+															+	+	+								4	16
B. DIPH- THE- ROIDES	+	- +	- +	- +	+	- +			+		+		+	+	+	+	+	+	+	+		+	+	+	+	20	800%
B. COLI		+											+													61	80%
STREP.	+					+										+	+	+		+	+	+	+	+	+	11	440%
N. H. STREP.								+		+			W.F.					+					+			4	160%
STREP.												*+														1	40%
STAPH. AUR.	+			+																						61	80%
STAPH.	+	*+	*+	+	+	+		+	+	+	*+	*- -	+	+			+	+	*+	+	*+	+	+	+	+	22	880%
MONTH OF GESTA- TION	10	10	5	10	4	4	ಣ	9	5	9	60	10	<u>r</u> -	4	10	9	ಣ	9	ಣ	9	4	ro Lo	00	20	20		
COLOR	W	W	M	M	В	В	В	W	M	W	В	м	W	M	M	M	M	В	щ	2	д	M	M	M	M		
AGE	26	59	23	31	27	25	21	21	25	22	22	24	23	56	23	23	23	22	50	55	50	19	28	27	28		
PATIENT	O. Mes.	М. Н.	E. H.	Н. С.	F.B.	R. J.	M. A.	E. B.	E.S.	M. M.	B. T.	N.C.	A. B.	D. T.	G. diM.	C. P.	M. B.	C. B.	R. G.	W.W.	L. H.	E. L.	I.B.	M.S.	E. R.	als	Dor cont
	1	67	က	4	10	9	1-	00	6	10	11	12	13	14	15	16	17	18	19	50	21	22	23	24	22	Totals	Dar

*Colonies hemolyzed blood agar.

c.c. concentration. All streptococci were collected by centrifuging the eighteen-hour growth obtained from cultures in becf infusion broth, pH 7.6. The remaining strains of organisms employed in the vaccine were grown on beef infusion agar slants. The eighteen-hour growth was washed from these slants with sterile normal saline, washed once and standardized as above noted.

Each of the separately collected vaccines was subcultured to blood agar to rule out contamination. The vaccines were then killed by the addition of sufficient 5 per cent alcoholic solution of thymol to make a concentration of 0.4 per cent thymol, and were stored at 6° C. overnight. On the following day each of the vaccines was diluted with an equal volume of sterile normal saline thus giving a concentration of 1 billion per c.c. These diluted vaccines were placed in sterile 60 c.c. vaccine bottles and tested for sterility by subculturing to blood agar slants, the latter being incubated aerobically and anaerobically for forty-eight hours. The bottles were then stoppered with appropriate rubber stoppers, the latter being sealed by the application of collodion. These vaccines were then properly labelled and stored continuously at 6° C. as stock suspensions of killed single type organisms from which a mixed vaccine could readily be made. The following outline summarizes the types of vaccine employed in the final mixed vaccine used in our studies (Table II).

TABLE II

	VACCINE	PROPORTION
	NO. OF STRAINS	PER CENT
1. Strep. hemolyticus	5*	35
2. Strep. viridans	8	15
3. Staph. aureus	2	15
4. B. coli communior	2	15
5. Strep. nonhemolyticus	4	10
6. Staph. albus	10	10

*Four of these strains were recently isolated strains; 2 were isolated from the blood and 2 from the lochia of patients with puerperal infections.

When it was found that all of these individual vaccines were sterile, we prepared a mixed vaccine, varying the percentage content of the various strains of organisms according to the above designated proportions. The desired quantity of each individual vaccine was removed from the "stock" bottle aseptically with a Luer syringe and hypodermic needle and the six fractions were pooled in a small sterile flask. An equal volume of sterile saline was then added to the flask and after thoroughly mixing its contents, this final preparation was transferred to 30 c.c. vaccine bottles. These were proved sterile by subculturing and further cared for by methods above noted.

It will be noted that the last saline dilution reduced the concentration of organisms to ½ billion per c.c., while at the same time the concentration of thymol was reduced from its original killing concentration of 0.4 per cent to a preservative concentration of 0.1 per cent. This concentration of organism and of chemical has proved satisfactory in a large series of cases observed by us. We can readily employ the necessary dosage with no demonstrable reaction attributable to the chemical preservative.

RESULTS OF TESTS ON ANIMALS AND NONPREGNANT WOMEN

It is considered inadvisable by some authorities to vaccinate women during pregnancy, but there was conspicuous lack of tangible evidence in the literature to substantiate this belief. However, before attempting vaccination of pregnant women, we employed the vaccine repeatedly in mice. We then vaccinated a series of non-pregnant women of childbearing age.

Twelve mice were divided into Groups A and B of 8 and 4 mice, respectively. Two experiments were conducted simultaneously on these groups. Group A was immunized by repeated injections of the vaccine, beginning with 0.1 c.c. and increasing the dose until nine injections had been given at regular intervals over a three-week period. The final dose was 1.0 c.c. and all mouse injections were given intraperitoneally. Ten days after the last injection, all mice of Group A were inoculated with a lethal number of living organisms obtained from young cultures of our isolated strains, one strain each of Strep. viridans and of Strep. hemolyticus being employed. This lethal dose was determined by inoculation of a series of nonvaccinated (normal) mice, when it was found that 0.5 c.c. of an eighteen-hour broth culture of streptococci was uniformly fatal in twelve hours or less. All of Group A survived, and two litters of apparently normal mice were found among these animals during the study.

Mice of Group B were subjected to single, large doses of vaccine intraperitoneally. Doses of 0.3, 0.5, 0.75, and 1.0 c.c., respectively, were given. As in Group A, these mice were observed for reactions. The two mice receiving the larger injections appeared to have a moderate reaction and were sluggish for several hours following the injection, in contrast to Group A mice which showed no reactions. However, on the days following vaccination Group B mice showed no evidence of untoward reaction and were normal in appearance. There was born a normal litter to Group B also.

Following our studies on mice, ten female patients who were already hospitalized were selected for study. These women were not pregnant, but were of the childbearing period, free from acute infectious diseases and well informed of the nature of the studies we wished to make. (Some of these patients were ambulatory while others were bedridden.) Careful records were kept in which the pulse, temperature, respiratory rate, blood pressure and urinalysis were recorded. They were observed especially for evidence of local or general reactions to the injections.

All of these women were first given an intracutaneous injection on the flexor surface of the forearm of 0.05 c.c. of the vaccine. Subsequent injections were given subcutaneously over the deltoid region at four-day intervals until a total of ten injections had been given each woman. The dosage was gradually increased from 0.05 c.c. to 1.0 c.c. at the tenth and final injection. Aside from an occasional complaint such as slight soreness at the site of injection or mild malaise, no untoward reactions were observed. Among this group of women were several postencephalities and cases of multiple sclerosis. Though this study was obviously not therapeutic in its aim, several of this group volunteered information to the effect that they had improved and felt better following vaccination.

VACCINATION OF PREGNANT WOMEN

The observations and results obtained by the vaccination of mice, and also of nonpregnant women of the childbearing period, were not only gratifying but encouraged us to proceed with the actual vaccination of the pregnant woman.

This study was conducted entirely on patients attending the antenatal clinics of the Jefferson and Philadelphia General Hospitals. Patients were accepted for vaccination irrespective of their past or present medical or obstetric histories, their acceptance depending only upon their willingness to cooperate in this study. Routine studies on these women consisted of the following: complete history and physical examination, urinalysis and blood pressure determination (at each weekly visit), blood Wassermann and Kahn tests. On many patients, in addition, complete blood counts and sedimentation tests were made.

This report includes the observations on fifty-one women in our series during the antenatal period, labor, and puerperium. Additional observations were also made on the babies born to these women.

Procedure (vaccination methods): All injections were given with tuberculin syringes and No. 26 gauge hypodermic needles, the skin at the site of inoculation first having been prepared by cleansing with sterile water and sponging with 95 per cent alcohol.

Each patient was first given an intracutaneous injection of 0.05 c.c. of vaccine on the flexor surface of the forearm, and then observed for local and general reactions at from one- to three-day intervals. Subsequent injections were at weekly intervals and were given intramuscularly in the deltoid region. The initial intramuscular injection was 0.1 c.c. (or 1.6 minims). Dosage was gradually increased by from 0.1 c.c. to 0.2 c.c. per injection. The total number of injections varied in the individual cases from a minimum of 3 to a maximum of 13 injections. The total volume of vaccine received during the course of immunization varied from 0.5 c.c. to 6.0 c.c. per patient.

Table III illustrates the total number of injections received.

A majority of the patients were vaccinated during the last trimester of gestation, most of the patients receiving all their injections during the last two months. Table IV illustrates the period of gestation when vaccination was given.

PATIENTS VACCINATED

Table V is representative of patients vaccinated, as to age, race, and gravida.

TABLE III

No. of injections	3	4	5	6	7	8	9	10	11	12	13
Cases	24	11	3	4	3	2	0	1	1	0	2

TABLE IV

Period of gestation	5	5-6	5-6-7	6	6-7	6-7-8	6-7	7	7-8	7-8-9	8	8-9	9
(months)				,			8-9						
Cases	0	1	1	0	0	2	1	1	1	2	6	19	17

TABLE V

Age	16-20		21-25		26-30)	31-	35	3	6-38
Cases	10	i	23		13		4		1 (38 yr.
Race White Negro	37 14									
Gravida	i	ii	iii	iv	V	vi	vii	viii	ix	x
Cases	17	14	5	4	4	2	1	2	1	1

It will be noted in Table V that of the fifty-one patients vaccinated, thirty-four were multiparas. Twelve of the latter group gave a history of one or more complications during their previous pregnancies. The complications were as follows:

COMPLICATIONS NO.	CASES	COMPLICATIONS NO.	CASES
Hypertension	1	Spontaneous abortion	2
Cardiac disease	1	Premature stillborn	1
Eclampsia	3	Vaginal plastic operation (1932)	1
Forceps delivery and stillborn	1	Induced labor	1
Uterine abscess (operated 1933)	1	Forceps delivery with a resultant	
Postpartum hemorrhage	1	rectovaginal fistula	1

There were nineteen patients with one or more complications during the present pregnancy. These were observed in the fifty-one vaccinated cases and were as follows:

COMPLICATIONS*

Badly diseased teeth	1	Gonorrhea	3
Toxemia of early pregnancy	4	Pyelitis	2
Trichomonas vaginalis	3	Preeclampsia	1
Hypertension, fall and separation of		Premature separation of placenta	
placenta (1 week before term)	1	with stillbirth	1
Profuse, foul vaginal discharge		Hypertension	1
(nonspecific)	4	Pulmonary tuberculosis (chronic)	1
Moderate, foul vaginal discharge		Rheumatism	1
(nonspecific)	1	Mitral stenosis	1
Placenta previa	1	Syphilis	1
Hip joint disease (shortening of		Condylomata acuminata	1
right leg)	1	Generally contracted pelvis	1

*No patient had more than two complications, either in the past or present pregnancies.

The types of complications observed in our vaccinated group are generally accepted as factors predisposing, either directly or indirectly, to puerperal infections. It is common knowledge that local or general complications during pregnancy bear an important relationship to the incidence of puerperal morbidity. The group of complicated cases in our study demonstrates the feasibility of vaccination with regard to tolerance in the pregnant woman with abnormalities.

The delivery of these patients should be considered very carefully. We deemed it unwise for the physicians in attendance to have knowledge of the prophylactic vaccination, since it was our aim to have different men deliver these patients under the same conditions and manner as is the custom with all ward patients. This was done only to aid in obtaining results that would be impartial and unbiased.

The diagnosis of presentation and position was made during labor and confirmed at delivery. The frequency of the various positions and presentations in the series is as follows:

POSITION	CASES	PER CENT OF TOTAL
1. L. O. A.	40	78+
2. R. O. A.	5	10-
3. R. O. P.	4	8-
4. L. O. P.	1	2-
5. Breech	1	2-

It is not within the scope of this paper to give in detail a description of the labor and delivery of this entire series. Table VI illustrates the incidence of certain features of delivery which, we feel, should be taken into consideration, since it is a known fact that the conduct of labor has a direct bearing on puerperal morbidity. Twenty patients in our series delivered themselves spontaneously and without complications. The remaining thirty-one cases had operative interference or one or more complicating features.

PUERPERAL MORBIDITY

Our criteria of puerperal morbidity are based upon the accepted standards in the two institutions in which these studies were made. The morbidity in the two institutions was 15.71 per cent and 22.32

TABLE VI

														CASE	NO	CASE NUMBER													
FEATURES OF LABOR	4	9	9	11 1	12 1	13 1	14 15	5 16	6 17	7 20	0 22	23	24	25	26	27	53	30	31	32 3	33 3	35 3	37 3	38 39	9 41	1 42	43	47	48
Febrile on admission		+	-	+	-	-	-	-	-	-	+	_	_					+		T	-	-	_	-	-	-	_	_	_
Bleeding antepartum	-	-	-	-	-	+	-	-	-	+	1	+								1	-	-	-	-	-	L	_	_	_
Labor induction	-	-	-	-	-	-		-	-	-	-	_			+					1		-	-	-	+	-	+	_	_
Premature rupture of membranes																			+			-		-				+	
Forceps	+	-	-		-	-	-	+	_	-			_								-	-	-	+	-	_	+		_
Version	_	-	-		-		-	-	-	-				_	+						-	-	-	-	_	_	_		
Episiotomy	+		+	+	_	-		-	_	+			_			+		+		+	+	-	+	+	_	+	_	_	+
First degree tear	-		-	-	-	-	-	+ - +	_	_	_	_	_	+			+				-	-	_	-	+			_	
Second degree tear	-		-		+	-	-	-	-	-		+	+								-	+	-	-	-	_	_	_	_
Postpartum hemor- rhage																							-	-	+		+		
Manual removal of placenta						-	+											+	-		-								
Totals	C1	1	_	01	1		1	1 2	61	1 1	-	0.1	-	1	61	-	1	00	1	П	1	1	1	63	1 2	-	60	_	1

per cent, for an average morbidity of 19.01 per cent. This represents the figures on all ward cases for the months during which our patients delivered (May to December, 1934, inclusive).

In our series of fifty-one vaccinated cases, there were only three cases (5.9 per cent) that were morbid during the puerperium. A description of these morbid cases is not amiss at this time.

Case 22.—A white patient, twenty-nine years of age, suffering from active gonorrhea and pyelitis at term. She had had two previous full-term babies. During the present pregnancy she received three injections of our vaccine at weekly intervals for a total of 0.9 c.c. of vaccine. She was admitted to the hospital four days after the last injection. On admission the patient was febrile. She delivered spontaneously in eighteen hours of a normal male child weighing 8 pounds 1¼ ounces. The position was L. O. A. She ran a febrile course until the seventh day postpartum. Five days later both mother and child were discharged in good condition.

CASE 30 .- A white patient, thirty-one years of age, in her second pregnancy. She had had one spontaneous abortion at six weeks. During the present pregnancy she received six injections of our vaccine at weekly intervals for a total of 1.8 c.c. of vaccine. She was admitted to the hospital six days after the last injection. Her temperature on admission was 101° F. She delivered spontaneously in eight hours and twenty-five minutes of a normal male child weighing 6 pounds 12 ounces. The position was L. O. A. The placenta failed to separate and was not removed until seven hours later, manual removal having been resorted to. The temperature fluctuated between 101 and 104° F., during which time there was complete urinary retention and catheterization was required. The urine was loaded with pus. Her blood culture was negative. On the sixth day postpartum the patient expelled a small accessory placenta (placenta succenturiata). Following the passage of this accessory placenta, the temperature returned to normal and remained so until the patient's discharge on the twelfth day postpartum. Both mother and child were in good condition when discharged. At the time of discharge, pelvic examination of the patient revealed the uterus to be well involuted, anterior and freely movable. There was no adnexal pathology.

Case 40.—A white patient, twenty-five years of age, in her second pregnancy. She had had one normal full-term baby. The patient suffered from chronic rheumatism throughout the present pregnancy. She was given four injections of our vaccine at weekly intervals for a total of 1.2 c.c. of vaccine. The patient was admitted to the hospital seven weeks after the last injection and delivered spontaneously in eleven hours and eight minutes of a normal female child weighing 8 pounds 1 ounce. The position was L. O. A. On the ninth and tenth days postpartum the temperature reached 101.5° F., though the patient had no complaints except for constipation. She was given a S. S. enema which was effectual, and her temperature dropped to normal and remained so. Both mother and child were discharged in good condition on the fourteenth day postpartum.

HOSPITALIZATION PERIOD

Fifty patients in our vaccinated series showed a variation from a minimum of six to a maximum of fifteen days hospitalization. One patient of the series who was delivered the eleventh time was kept in the hospital four weeks. This patient (Case 26) suffered from chronic fibroid tuberculosis and marked diastasis recti. She was sterilized, her appendix removed and the diastasis repaired. She left the hospital, much improved, fifteen days following operation.

The average number of days of hospitalization in fifty patients was 9.6. Table VII shows the number of days of hospitalization for this group.

TABLE VII

Days in hospital	6	7	8	9	10	11	12	13	14	15
Total cases	2	2	9	10	18	2	4	0	2	1

BABIES BORN OF VACCINATED MOTHERS

A study of these vaccinated patients would not be complete unless it included observations made on the newborn. There were 26 males and 25 females. The weights varied from 4 pounds 6 ounces to 9 pounds 5 ounces, the average weight being 7 pounds 4.1 ounces.

In the entire group there was but one abnormality (supernumerary digit on the radial aspect of the right hand). This was operated upon successfully, and the infant was discharged in good condition on the tenth day.

There were 50 livebirths and one stillbirth in the group, giving a fetal mortality of 1.96 per cent. The stillbirth occurred in a white primipara, twenty-eight years of age. She suffered from preeclamptic toxemia and subsequently developed a premature separation of the placenta. She was delivered spontaneously at term of a stillborn male child after twenty-one hours and forty minutes of labor. This mother (Case 23) received three injections of our vaccine at weekly intervals for a total of 0.6 c.c. of vaccine. The last injection was given eight days prior to delivery. When this woman was first observed by us, she had hypertension and edema. We do not feel that the ultimate outcome of this case bears any relation to the previous vaccination.

DISCUSSION

We feel that this study is of particular interest and importance, since we believe that anything that is able to influence the incidence of puerperal infections is worthy of careful consideration.

When we consider the figures as presented by Adair, who states that of 7,380 obstetric deaths, 40 per cent were due to sepsis, is it any wonder that there is much room for improvement, no matter how slight that improvement may be? It is not only the fatalities due to puerperal infections that harass the obstetrician, but also the resulting invalidism and the subsequent mutilating operations that are often required among those fortunate enough to survive.

Therefore, we feel that a vaccine that tends to increase the resistance of the pregnant woman against puerperal infections is of paramount importance. Of course, it would be ridiculous for any one to say that puerperal infections could be abolished entirely and forever, but on the other hand, it is not impossible that such infections may be reduced to a minimum.

Although our series consisted of only 51 cases, yet we feel that there was ample opportunity to observe the effects and workings of this vaccine. As stated before, our patients were not hand picked. In reality, they represent a cross-section of the average obstetric

practice with its associated complications such as may be observed in primiparous and multiparous women during pregnancy, labor, and the aerperium.

I'ne safety of the vaccine was proved beyond a doubt, both in pregnant and nonpregnant women. We feel that the absence of abortions and miscarriages is a significant feature of this study.

The vaccine was administered to pregnant women with various complications in addition to their pregnant state. These complications varied in type and severity, and yet we failed to observe a single case that presented an aggravation of the preexisting condition.

There were several cases that we will mention since we feel that they will demonstrate some of the advantages of vaccination.

Case 43.—White woman, aged twenty-six years, primipara. Complication during pregnancy Trichomonas vaginalis. This patient during pregnancy received thirteen injections of vaccine for a total of 6.0 c.c. Two attempts to induce labor failed. This patient was overdue. The position was L. O. A. Finally she went into labor and after twenty-nine hours and thirty minutes she was delivered by a low midforceps operation and a medio lateral episiotomy. The child was a male, living and well, weighing 8 pounds 8 ounces. There was an immediate, severe postpartum hemorrhage. The patient required, in addition to the immediate remedial measures to control the hemorrhage, a blood transfusion, receiving 430 c.c. of whole blood. At no time during the puerperium did this patient have fever, and she made an excellent recovery, leaving the hospital on the twelfth day.

Case 41.—White woman, aged twenty years, primipara, no complications during pregnancy. This patient received eight injections of vaccine for a total of 3.6 c.c. Surgical induction was performed as the patient was overdue. The position was L. O. A. She went into labor and delivered spontaneously sixteen hours later. The child was a female, weighing 5 pounds 13 ounces, living and well. There was an immediate postpartum hemorrhage which was later controlled, but the patient had to be transfused. She received 350 c.c. of whole blood, yet at no time during the puerperium was she febrile and was discharged from the hospital on the twelfth day in good condition.

CASE 14.-White woman, aged thirty years, para ii; complication during this pregnancy: moderate vaginal discharge, mild toxemia of early pregnancy. She received three injections for a total of 0.5 c.c. She was delivered spontaneously at term in eleven hours and three minutes of a male child weighing 9 pounds 5 ounces. The placenta could not be delivered spontaneously, and after waiting, the diagnosis of adherent placenta was made. The placenta was removed manually and the uterus packed with iodoform gauze. At no time during the puerperium was this patient febrile, and she was discharged on the tenth day in good condition.

CASE 17.-Negro woman, aged nineteen years, para ii; complication during pregnancy: bleeding during eighth month, lateral placenta previa. She received during her pregnancy seven injections of vaccine for a total of 3.3 c.c. She went into labor; the position was R. S. A. (footling). During labor the cord prolapsed and was replaced manually, and after twenty-two hours and twenty minutes she was delivered of a male child, living and well, weighing 6 pounds 5 ounces. At no time during the puerperium was this patient febrile, and she was discharged on the ninth day in good condition.

Case 26.—White woman, aged thirty-five years, para x, had had eclampsia with her first child. The complications during this pregnancy were hypertension on admission (blood pressure: 180 systolic, 120 diastolic) and chronic fibroid tuberculosis. This patient received three injections for a total of 0.5 c.c. of vaccine. On account of her condition, the membranes were ruptured artificially to induce labor. The membranes were ruptured for fifteen hours before the onset of labor pains. When the cervix was completely dilated, internal podalic version had to be performed, the aftercoming head forceps were employed, and the patient was delivered of a female child, living and well, weighing 6 pounds 4 ounces. At no time was this patient febrile. She made a good recovery, and four weeks later she was sterilized; and fifteen days following sterilization she was discharged.

The five cases noted above, though only a fraction of the abnormal group shown in Table VI, are sufficient to convince us that vaccination of pregnant women is advantageous. At the same time, as one may observe after studying our results, it will be noted that deleterious effects on either the mother or child are conspicuous by their absence.

After a consideration of the hospitalization period in our series, we believe that the 9.6 day average compares favorably with that of other institutions.

SUMMARY

The appalling mortality and morbidity due to puerperal infections prompted us to carry out the investigations just described.

A method has been presented whereby a suitable vaccine was prepared and used in an attempt to immunize a series of fifty-one pregnant women.

The following points may be considered salient features of this study:

- 1. Active immunity was conferred to mice by means of repeated injections of vaccine.
- 2. The safety and absence of reactions to the vaccine were first demonstrated in a series of nonpregnant women of the childbearing period.
- 3. Fifty-one pregnant women were given from three to thirteen injections of the vaccine without untoward reactions.
- 4. In the entire series of fifty-one cases, there was not observed a single abortion or miscarriage.
- 5. Preexisting conditions in these cases, whether acute or chronic, were not aggravated by vaccination.
- 6. These fifty-one patients delivered with no fatalities. The puerperal morbidity was 5.9 per cent as compared to the combined morbidity of the nonvaccinated cases which was 19.01 per cent.
- 7. There was one stillbirth in our series, the mother being a preeclamptic patient with marked hypertension and a separated placenta.

We feel that this type of vaccination of pregnant women should be included in our armamentarium of prenatal care.

We wish to thank William Richman, B. S., for his valuable assistance.

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SINGLE CONTRACTION DELIVERY IN BREECH PRESENTATION

E. T. RULISON, B.S., M.D., SACRAMENTO, CALIF.

IN THE registration areas of the continental United States of America I the annual recorded live-births during the years 1928 to 1932 averaged 2,160,000. Of this number approximately 64,800 were breech babies, as the incidence of breech presentation in any large series of deliveries has been found to be approximately 3 per cent. The average fetal mortality in breech presentation at term is difficult to ascertain as our reports emanate from the maternity clinics of university hospitals for the most part, and the total number of babies delivered in these institutions is but a small fraction of the actual total, probably not more than 5,000 or 6,000 infants yearly. Inasmuch as the known average fetal mortality of fourteen reporting American clinics is in the neighborhood of 11 per cent, it is probable that the mortality rate of the larger group of 55,000 to 60,000 cases in the hands of presumably less skilled operators would reflect a much higher rate. Hegar,² for instance, reports a 40 per cent mortality in the country districts of France, and Gibberd³ believes the mortality in average district practices in England is still about 40 per cent. Fetal mortality incident to breech deliveries in the three Sacramento hospitals during the year 1934 was 16.2 per cent. If we accept 20 per cent as a fair average mortality throughout the United States, we arrive at an unpleasant total of approximately 14,000 babies who perish yearly as the result of pelvic presentation.

The challenge to reduce the staggering death rate in breech presentation has been accepted by American obstetricians as will be evident by the review of the excellent contributions of Goethals,⁴ Sherman,⁵ Davis,⁶ Studdiford,⁷ Schwarz,⁸ Wilson,⁹ Piper and Bachman,¹⁰ Cornell¹¹ and others. The problem resolves itself, as many writers have so pertinently emphasized, into two general considera-

tions: First, the conversion of the more hazardous pelvic to the less hazardous cephalic presentation; and second, improved technic in the management, both antepartum and intrapartum, of the persistent cases and those not recognized until labor has begun.

Burns,¹² in a recent contribution remarks: "That new principles of treatment have not been expressed and that each writer has simply perpetuated the teachings of his predecessor is clearly evident from a perusal of the textbooks published during the past twenty or thirty years. On no important point does the treatment ever appear to be questioned, and the paucity of new ideas is everywhere remarkable."

A review of the contributions of the American authors already mentioned constitutes an answer to the lament of Burns and, while one may not be in agreement with some of the proposed changes in management, there is ample evidence that abundant conscientious thought and endeavor has been and is being directed to the problem. During the past twenty years prophylactic external version has gained acceptance as a reasonably safe maneuver and one that is successful in 70 to 80 per cent of cases when attempted between the thirty-second and thirty-sixth week of pregnancy.

Donovan¹³ lists as contraindications to external version: (1) antepartum hemorrhage, (2) placenta previa, (3) fibromyomas, (4) contracted pelvis. Resulting transverse presentation has been noted and in my experience the resulting vertex presentation frequently has been an occipitoposterior position which led to protracted labor. The mechanism of the resulting occipitoposterior position following external version is apparent from a study of the illustrations accompanying Davis¹⁴ article. It is probable, however, that the average accoucheur would prefer to accept the responsibility of an occipitoposterior position to that of a sacroanterior position.

Goethals¹⁵ has drawn attention to the advisability of x-ray pelvimetry and cephalometry in the known persistent breech presentations, both in primiparas and multiparas. Control measurements indicate a possible accuracy within 5 mm. in 100 per cent of cases and 3 mm. in 75 to 95 per cent of cases. An absolute indication for cesarean section was found in one of his cases.

The succinct advice as to management during labor so admirably stated by Wilson¹⁶ is a crystallization of the advances made during recent years. In the ordinary type of breech presentation Wilson stresses the following points:

Careful diagnosis of the presentation and accurate pelvimetry;

Gentle attempts at external version;

Avoidance of unnecessary examinations for fear of rupturing the membranes prematurely:

During labor an attitude of watchful waiting, with an anesthetic, preferably nitrous oxide, administered to the point of analgesia only,* preparation being made in the meantime for immediate interference, if necessary;

Careful observation of the patient's general condition and the rate and rhythm of the fetal heart;

Episiotomy* as the breech distends the vulva;

^{*}Italics by the writer of this article.

Complete anesthesia for the delivery of the head, either spontaneously or manually, assisted by steady but moderate pressure from above. These presentations should not be subjected to manual extraction as a routine.

I am in accord with all points made by Wilson with the exception of the use of complete anesthesia and abdominal pressure on the after-coming head.

Bearing on this point Cornell¹⁷ states: "If we wish the patient to deliver the head promptly we must not give an anesthetic to the point where she is uncooperative.

Sherman¹⁸ in his splendid contribution is most apposite in saying: "What should be taught is how to properly handle a breech when confronted with one and how to make the presentation a less difficult one. Since the fetal mortality in 75 per cent of the cases is due to injury to the fetus, rather than asphyxia, it is felt that the policies advocated by Polak, 'let her push and you guide' and by Caldwell and Studdiford 'hands off as long as labor is advancing' should be followed. Less haste and interference on the part of the physician will minimize trauma to the fetus and mother. Frantic haste is not necessary, but careful, deliberate, unwasted movements are essential." Sherman lists the following indications for interference: fetal or maternal distress, impacted breech, tonic uterus, no advance with full dilatation for three hours, and no advance into the inlet in slightly contracted pelvis. He condemns operative interference as a routine to lessen fetal mortality. With DeLee he questions whether an infant mortality of 6 to 10 or even 15 per cent justifies an operation which has a 2 to 16 per cent maternal mortality. In teaching services he advocates careful supervision by the attending staff, considering even spontaneous delivery an operative maneuver. Sherman advocates the semi-Walcher position for delivery, episiotomy, anterior or posterior delivery of the upper extremities, and the Martin-Wiegand technic as least dangerous in delivery of the after-coming head. He refers to anesthesia as a factor making delivery of the head easy or difficult but unfortunately does not elaborate this point.

A review of the contributions pertaining to breech presentation during the past ten years leaves one very well satisfied that the subject has been quite exhaustively handled from the point of view of breech extraction. Breech extraction, however, is synonymous with interference, with its consequent higher fetal mortality. The increase of successful breech deliveries or, conversely, the lessening of the incidence of breech extraction is the problem awaiting solution. It would seem that there should be more contributions emphasizing the points leading to successful breech delivery and less of the defeatist type detailing operative methods designed to eliminate or modify the second stage of labor. While the fetal mortality in certain clinics probably may be lowered by such radical methods, one must remember that probably 90 per cent of breech cases are in the hands of general practitioners and individual obstetricians throughout the country. To them proposals to eliminate the second stage by proceeding with breech extraction in all cases upon completion of cervical dilatation or to deliver by cesarean section all parturients irrespective of parity with fetuses of an estimated weight of eight pounds or more, are fraught with the danger of greatly increasing fetal mortality and

maternal morbidity. There is a fear complex evident in the minds of scores of practitioners dealing with occasional breech cases, and in my opinion it is the consideration of the many articles detailing refinement of technic in breech extraction and advocating radical procedures which engenders and fosters this unhappy state of mind. The fear of fetal mortality in the minds of obstetricians in private practice is such that elective cesarean sections are frequently advised and consummated in primiparous patients with normal pelvic measurements and average sized fetuses. The attitude of these men is due to a repetition of unhappy experiences, the conscientious care of the patient over a period of months ending in disaster for the baby after a few short hours of labor. No obstetrician is pleased with the diagnosis of breech presentation. His experience with external version is often unsatisfactory for the reason that the resulting vertex presentation frequently proves to be a persistent occiput posterior, subjecting his patient to a hard protracted labor.

The design of this paper will be fulfilled if in any degree a sense of confidence in the successful outcome of breech presentations may be instilled in the minds of obstetric practitioners. No claim to originality in the successive steps of the management of breech delivery to be detailed may be made with one possible exception. During a period of twenty-two years' practice of obstetrics an attitude of extreme uncertainty as to the outcome has gradually changed to a fair degree of confidence. The higher fetal mortality of the first five years was due not so much to inexperience as to an improper conception of the problem of management established during student and interne years. My conviction is that the salient points in successful breech delivery were not stressed in training, and I am certain that the same condition obtains today in many of our best schools and maternity hospitals. The younger obstetricians are now observed to be passing through the same unhappy ordeals that were my share twenty years ago. It has been said of certain eminent cataract surgeons that their success was attained through the sacrifice of a "hatful" of eyes. Must the obstetrician be faced with the necessity of sacrificing a number of babies? The departments of obstetrics in some of our schools and the staffs of certain of our maternity hospitals are unconsciously but certainly sending forth men yearly with astigmatic vision of this problem. The faulty attitude of many of these men at the beginning of their obstetric work is in a large measure the result of failure to recognize that the conduct of labor in breech and cephalic presentations should be disparate in several important essentials.

The first normally rapid breech birth which I witnessed was that of a Japanese woman in the hands of a midwife. The beautifully easy and rapid mechanism of delivery with the patient awake and in full

possession of her expulsive forces was most impressive and prompted an immediate change in my attitude and management of these cases.

If delivery of breech cases is to be repeatedly successful the presentday obsession for total amnesia and analgesia through the administration of drugs which in the slightest degree interfere with uterine contractions and abdominal expulsive forces, not only must be restricted but entirely overcome. Judicious use of certain analgesic drugs may be employed to advantage in the occasional case which tends to early exhaustion by reason of an unstable nervous organization. But, as DeLee19 says: "Time and pain are secondary considerations in normal cases. It is the demand of the doctors and patients for quick, painless labors that keeps up the high fetal and maternal mortality in the United States." Interference with the expulsive forces summons the chimera of impaction; and the usual "relief" of "impaction" by bringing down one or both legs, followed by breech extraction, spells disaster in many instances. A study of the statistics in breech presentations indicates clearly that fetal mortality is entirely proportionate to the use of analgesic drugs and interference, both manual and instrumental.

AUTHOR'S TECHNIC

Prenatal Care.—One element in prenatal care has not been sufficiently stressed, namely, consideration of the increase in maternal weight. This should be carefully watched in all primigravidas regardless of presentation, with the purpose in mind of limiting the fetal weight to an extent commensurate with safe passage through the birth canal of the individual patient. The principles involved are commonly known and not within the scope of this paper.

The writer assumes in the management of delivery herein detailed that no disproportion has been determined by x-ray or other observation in the diameters of the pelvis or the fetal head.

Management During Labor: First Stage.—The management of the patient in the first stage of labor is not affected by the diagnosis of the four positions of pelvic presentation, nor by the variation in the attitude of the lower extremities of the fetus, whether complete, frank, or half breech.

Early rupture of the membranes necessitates an immediate examination of the patient to determine the presence or absence of cord prolapse. If present, its replacement of course should be attempted at once by the usual methods. The facilities of a good hospital delivery room are not essential but highly desirable, especially in primiparas. The patient should be prepared locally according to the standardized maternity routine, including cleansing enemas. Vaginal instillation of 8 c.c. of 1-500 metaphen solution or 3 per cent mercurochrome every eight hours according to Mayes' technic may result in possible lessening of morbidity during the purperium. The patient should be confined to her bed during the first stage of labor with a view to the better preservation of the membranes. Abdominal and rectal examinations should be made at intervals deemed advisable by the attendant. Liquid nourishment may be given every two or three hours.

The patient should be informed that her baby is coming "foot first" to insure her full cooperation. In private practice patients have learned to expect drugs and anesthetics to alleviate the pains of childbirth. It is well in breech cases to discuss

the situation frankly with the patient but in a manner not to cause alarm or apprehension. The patient should be told that the baby may be born "foot first" safely in most instances, but that the breech is soft and does not dilate the parts quite as rapidly as the head. She is told that it is therefore important that nothing should be given in the way of drugs to interfere with the natural contractions of the uterus or the voluntary bearing down in the final stage of birth. The patient should be assured, however, that "gas" will be given before the baby is born.

Second Stage.—The patient should be under the obstetrician's observation in the delivery room throughout the entire second stage. If the presenting part makes satisfactory progress in its descent, the patient may be left to her own devices as to position and bearing down efforts. At times it is advisable to place the patient in an extreme lithotomy position and coach her carefully, pain by pain. The mentality and behavior of the individual patient differ widely; therefore the attendant must decide which method of handling will best conserve maternal energy. During the last hour of the second stage the anesthetist may be present and prove to be a source of comfort to the patient. The anesthetist, however, must completely abandon any preconceived ideas of analgesia or anesthesia. It is absolutely necessary that the obstetrician specify the percentage of nitrous-oxide-oxygen to be used. Theoretically, nitrous-oxide-oxygen analgesia does not impair the expulsive forces, yet how many times in actual practice have we seen a progressive advance of the presenting part arrested soon after the ministrations of the anesthetist? A mixture of 40 per cent nitrous-oxide and 60 per cent oxygen admittedly will not produce a satisfactory analgesia, nor will it interfere with the back-log of maternal energy necessary for the final step in delivery. Five or six inhalations at the onset of each contraction, however, does satisfy the patient that an effort is being made to alleviate her distress.

In the case of a frank breech with an apparent disproportion between the size of the fetus and the birth canal, experience and careful observation of the condition of the mother and fetus at frequent intervals become the obstetrician's best allies. A most refined judgment is at times necessary to determine the timing of interference should impaction threaten. Impaction is synonymous with maternal exhaustion. Maternal exhaustion imposes upon the obstetrician the mandate of breech extraction with its multitude of attendant evils. Patience and the reflection that, while the breech is a poor dilator, nevertheless dilatation will occur in most instances if nothing has been done to detract from the efficiency of the expulsive forces, frequently lead to a happy, spontaneous, safe delivery. The notion that extended legs act as splints, thereby preventing lateral flexion and progressive descent, has been responsible for many instances of needless interference. Jardine²⁰ has pointed out that "for the lower extremities to act as splints they must be rigid and fixed at both ends. They are not fixed at the lower ends and it is possible for the lower extremities to bend laterally at the knees sufficiently to allow lateral flexion." The patient is coached with each pain to "bear down" and as the presenting part begins to distend the perineum, the latter may be ironed out digitally, care being taken not to permanently damage the fascial planes or cause submucous tears of the perineal muscles.

The patient's bladder should always be thoroughly evacuated by catheter as the presenting part comes in view. It is advisable of course to have obstetric forceps and resuscitation paraphernalia at hand in event intervention becomes necessary. The management of the delivery from the beginning of perineal distention becomes one of exact timing step by step. As the presenting part in its advance begins to swing ventrally beneath the pubic arch the patient should be given primary nitrous-oxide-oxygen anesthesia to permit mediolateral episiotomy by scalpel. Infiltration of the perineal skin, vaginal wall and deeper tissues with 1 per cent novocaine is

an excellent alternative to primary gas anesthesia. In the case of the right-handed obstetrician, the episiotomy naturally will be to the patient's left. Episiotomy on the side to which the presenting sacrum points is a refinement stressed by some authors. The depth of the episiotomy is determined by the estimated size of the fetal head, the width of the outlet and the character of the musculature of the perineum. In primiparas and multiparas with virginal type of perineum, the incision should be a generous one, carried even into the levator ani muscle if deemed necessary. As DeLee21 has emphasized so well: "It saves delay in the delivery of the shoulders and head and surely has saved many babies' lives as well as prevented complete lacerations of the perineum." The anesthetic is stopped immediately following the episiotomy, and time is allowed for satisfactory resumption of expulsive pains. The presenting part is kept covered by the customary hot towel, although as Gibberd22 remarks: "It is unnecessary in an easy case, an impediment in a difficult one, and probably in no case does it prevent inspiration by the fetus." A hypodermic injection of Infundin (mm. iii) or obstetrical pituitrin (mm. vi) may now be given to insure more efficient and better sustained contractions.

The writer offers as his opinion that the design for the actual delivery of the baby in the normal uncomplicated case should be birth from breech to and including head during the period of a single contraction. The stage must be carefully set for this final maneuver which in time is a matter of seconds only. The patient lies in a lithotomy position with high stirrups or in a semi-Walcher position with the lower extremities in saddle stirrups as recommended by Piper and Bachman, Sherman and others. The semi-Walcher position undoubtedly relaxes the perineal muscles and increases the anteroposterior diameter of the inlet, both considerations being of importance at this juncture. Some women, however, are less successful in consistently advancing the presenting part in their expulsive efforts in this position. anesthetist is now giving straight oxygen with each pain. The uterine contractions are becoming more and more forcible as the pituitrin effect is established. The nurse is not permitted to touch the abdomen and the obstetrician should not be annoyed immediately before delivery by an attendant detailing the character or rate of the fetal heart. He should be the sole judge of the onset and character of the contractions. The presenting part is easily restrained and may be permitted to come well through the outlet and pushed back without endangering the fetal circulation. This maneuver insures complete effacement and paresis of the cervix and lower birth canal. The crucial moment arrives when the contraction has a maximal, well sustained, expulsive force. The patient is now instructed to bear down well and continue to bear down. The breech and lower extremities are received and at the emergence of the cord, a loop is drawn down gently. Manual aid is always given to accomplish the delivery of both arms as it is time saving. It is greatly simplified as a result of the episiotomy. As the scapulae come into view the body is gently swung laterally and the posterior arm swept out by the homolateral hand of the operator. Rotation to bring the anterior arm into the hollow of the sacrum is then done, to the left or right depending upon the original position, and the second arm is delivered. Manual aid in delivery of the arms is surprisingly amplified by the continued advance of the baby due to the sustained uterine contraction and the continued voluntary bearing-down effort of the patient. The emergence often assumes a moderately projectile character although this is probably more apparent than real. The delivery to this point should be accomplished while the pain is but reaching its height. The head is still within the uterine cavity; the contraction of the uterine musculature in its climactic period expels the head into the vagina. Expulsion of the head into the midpelvis is aided by momentarily allowing the fetus to hang downward. As Burns23 has pointed out, this maneuver permits the shortest diameters of the fetal head, the occipitofrontal and occipitobregmatic, to roll downward through the brim, adequate head flexion being assured. It now remains merely to lift the child by the feet, using the left hand while guarding the perineum with the right, and delivery is complete. In lifting the child it is held by the ankles and the obstetrician's left hand swings upward through an arc of about 180 degrees. With the patient consciously bearing down, no tension or traction on the body is required. Rather is it necessary to focus attention on the protection of the perineum, as the head in many cases advances forcibly. While the rapid delivery of the head following the appearance of the mouth is not imperative, there is likewise no particular advantage in a slow delivery if an adequate episiotomy has been performed. The usual time consumed for cord to head delivery is rarely over thirty seconds, and many deliveries have been effected in fifteen to twenty seconds. In a recent case of a primipara with a minor degree of justominor contraction, the baby weighing 7 pounds 10 ounces was delivered from cord to complete birth of head in ten seconds without apparent injury to baby or mother.

The management detailed above pertains, as stated previously, to cases of breech presentation in primiparas or multiparas with normal pelves and soft parts and average sized fetuses. The elderly primipara with long rigid cervix, the parturient with placenta previa complicating breech presentation, fetal hydrocephalus, and monstrosities are not within the scope of this paper and, of course, require treatment and maneuvers which are well standardized. The use of hydrostatic intrauterine bags in the group of cases with slowly dilating cervices is a logical one, obviating in many instances a recourse to cesarean section.

One logically may ask what steps should be taken in the event delivery is not completed during a single contraction. Rather than risk asphyxia by awaiting subsequent contractions and hoping to effect a spontaneous delivery, it would seem wiser to proceed at once with a breech extraction under gas anesthesia. The Martin-Wiegand principle recommends it as the safest effective technic. Briefly, it consists in guiding the head through one of the oblique diameters of the inlet by suprapubic pressure of one hand while the thumb and fingers of the opposite hand maintain head flexion and exert traction. The face grip consists of thumb beneath chin and fingers on malar bones, the fetal body riding the forearm. This method of delivery of the aftercoming head failing, immediate recourse to forceps of the Piper-Bachman type should be had.

PROSPECTIVE CRITICISM

It is anticipated that objection may be raised to the method of single contraction breech delivery. The criticism that immediately occurs to the mind of the obstetrician is that delivery is too rapid, precipitate in fact. We have been schooled in the avoidance of haste in delivery of the after-coming head. The warning to avoid haste and undue traction on the after-coming head is well founded, as the fear of fetal death while the nurse counts off the minutes after the appearance of

the cord often prompts the accoucheur to the use of undue force. This frequently results in the rupture of the tentorium cerebelli with intracranial hemorrhage, injury to the cervical spine or injury to the roots of the brachial plexus. In single-contraction breech delivery the after-coming head is expelled by a competent, evenly distributed vis a tergo. It is probably not much greater than the pressure to which the head has been subjected by the preceding second stage contractions. It is not unusual in vertex presentation for delivery to be effected during a single uterine contraction. Why then should it not be permissible to encourage delivery during a single uterine contraction in pelvic presentation? The advantages inherent in such a method seem patent. The absence of asphyxia and postnatal cerebral complications furnishes proof that the method is not injurious to the baby. Many of these babies have been under observation over a period of several years.

Another criticism that may be offered is that the rapid delivery may predispose to premature separation of the placenta and to postpartum hemorrhage. While my experience has been confined to my private cases and is therefore limited, the method has been used in its present form for several years and no instance of serious postpartum hemorrhage has been encountered. It has been my observation as well as that of many others that the placenta separates somewhat earlier than in cephalic presentation and there are, no doubt, many instances of premature separation. Intrapartum placental separation is rather an argument in favor of single contraction breech delivery inasmuch as the fetus is delivered in a few seconds and thus is not exposed to asphyxia which so often occurs during more protracted birth.

Does the method predispose to rupture of the perineum? If an adequate episiotomy has been performed no fear need be had of any laceration whatever. Delivery of the head following emergence of the mouth may be as slow and deliberate as the individual operator may elect.

Another query that is certain to be advanced is: "Why deliver the baby in thirty seconds when authorities agree that four minutes (Tweedy-Wrench) to twenty minutes (Potter) may elapse before the fetus develops asphyxia?" The writer elects the feminine manner of replying to this by countering: "Why consume valuable minutes with their attendant period of apprehension on the part of the accoucheur and distress to the patient if only a few seconds are necessary?" We must remember that the success of this method of delivery rests upon the premise that the patient remain conscious and cooperative, and accordingly a birth as rapid as is compatible with the safety of mother and child is indicated.

Finally, has there been complaint on the part of mothers that they have been forced to suffer unnecessarily? No such complaint has been registered by any of my patients. If such were the case, there may be justification in the fact that the pains of childbirth are soon forgotten, but the wound inflicted upon the mother by the unhappy intelligence of her baby's failure to survive is one which requires years to heal.

SUMMARY

Approximately 65,000 breech babies are born yearly in the United States. About 14,000 of these perish as a result of pelvic presentation.

As the great majority of these are delivered by private practitioners, management to increase the percentage of spontaneous deliveries is desirable.

A review of cases encountered in private practice over a period of twenty-two years is used as the basis of this contribution.

ESSENTIAL CONSIDERATIONS IN SINGLE CONTRACTION BREECH DELIVERY

- 1. Prenatal dieting and exercise to avoid an oversized fetus and to promote the best possible physical condition of the mother. This, of course, applies to all parturients.
- 2. Avoidance of analgesic drugs during the first stage of labor in the average normal case; judicious use of these agents in the occasional case which tends to early exhaustion due to unstable nervous organization.
 - 3. Careful coaching by obstetric attendant during expulsive pains.
 - 4. Delivery in lithotomy or semi-Walcher position.
- 5. Subanalgesic nitrous-oxide-oxygen (40 per cent nitrous-oxide, 60 per cent oxygen) during pains of the last hour. One hundred per cent oxygen immediately preceding actual delivery.
- 6. Liberal mediolateral episiotomy as perineum reaches full distention, performed by scalpel under transient gas anesthesia or novocaine infiltration.
 - 7. Administration of obstetric pituitrin or infundin.
- 8. Delivery during the period of a single maximal, well-sustained contraction, accurate timing being of primary importance.
 - a. Delivery of lower extremities, torso and upper extremities before contraction has reached its climax; routine manual aid in the delivery of arms.
 - b. Momentary dependent position of fetus as after-coming head is expelled by uterine contraction into the lower birth canal.
 - e. Delivery of head by raising fetus through an arc of 180 degrees by the left hand, as perineum is guarded by the right hand.

STATISTICAL DATA (MY CASES)

Breech presentation has occurred in 5 per cent of my cases. There were twentytwo instances in primiparas and twenty-one in multiparas. Prophylactic external version was successful in five cases in multiparas and failed in two cases in primiparas. Spontaneous delivery occurred in 68 per cent of the 43 cases. Since the adoption of the management above described in the full-term group of twentysix cases delivered per vaginam there has been a loss of one baby, a fetal mortality of 3.8 per cent. In this instance, the mother, a preeclamptic primipara, not under my prenatal care, entered the hospital after fourteen hours of labor, fully dilated with membranes ruptured and fetus showing signs of distress. Delivery was accomplished under ether anesthesia by breech extraction. Two patients were delivered by cesarean section, the indication being large fibromyomas in one, contracted pelvis in the other. In the total group of forty-three cases, including four patients delivered at a period of gestation from the twenty-eighth to the thirty-second week, and five pattents delivered following prophylactic external version, seven babies failed to survive, a fetal mortality of 16.3 per cent. One death occurred in utero following an easy external version. A macerated fetus was delivered twenty-five days later. Placental disease rather than external version was undoubtedly responsible for the death of the fetus. The delivery mortality of the total group was 11.6 per cent. Excluding the four premature cases and the five patients delivered following external version, there were three deaths or a mortality of 8.8 per cent. Two of these patients were delivered by breech extraction following conduct of labor by midwives. One patient had been in labor for eighty hours.

The maternal mortality was nil.

The average fetal weight in the twenty-five full-term cases without mortality, delivered according to the methods described, was 7.4 pounds in primiparas and 7.9 pounds in multiparas. One primipara was delivered of a fetus weighing 9 pounds 4½ ounces; one multipara was delivered of a fetus weighing 10 pounds 9 ounces. The average duration of labor in this group was 14.6 hours in primiparas and 16.6 hours in multiparas. Excluding the case of protracted labor of seventy-two hours in one of the multiparas, the average duration of labor in this group was 10.5 hours.

ANALYSIS OF INTRA- AND POSTPARTUM FETAL DEATHS

Hydrostatic bags were used in nine of the 43 cases, or 20 per cent.

	PRIMIPARAS	MULTIPARAS
Premature, spontaneous	1	1
Full term, breech extraction	2	1
Full term, following external version		1
Total: 6 deaths in 43 cases		

PREMATURE SPONTANEOUS

Case 1.—Multipara (Grav. iii), aged thirty, eclamptic in twenty-eighth week of pregnancy; induction of labor by Voorhees' bag; convulsion eight hours before delivery was probable cause of death in utero; fetal weight 4 pounds, length 41 cm.

CASE 2.—Primipara, aged twenty-seven, in the thirty-second week of pregnancy; injured by accidental blow on abdomen a day previous to onset of labor; spontaneous delivery; fetus died forty-five minutes after birth. Autopsy disclosed no brain injury; congenital absence of right kidney; fetal weight 5 pounds 5 ounces.

FULL TERM-BREECH EXTRACTION

Case 1.—Primipara, aged thirty-five, spontaneous rupture of membranes five hours before onset of pains. Full dilatation after seven hours' labor. Interference by

bringing down both feet. Breech extraction under ether anesthesia. After-coming head delivered by forceps. Weight of fetus 8 pounds. This patient was delivered in 1913.

Case 2.—Primipara, aged twenty-eight, preeclamptic delivered by breech extraction under ether anesthesia after fourteen hours' labor. Under midwife's care before admission to hospital. Indication for breech extraction preeclamptic condition of mother and signs of fetal distress. Difficulty experienced with extended arms and after-coming head. This patient was delivered of breech babies in three successive years. The second and third deliveries were spontaneous, the babies weighing 8 pounds 9 ounces and 10 pounds 9 ounces, respectively.

CASE 3.—Multipara (Grav. x) under midwife's care for eighty hours. Impacted frank breech; mother exhausted. Breech extraction under chloroform, home delivery. Heart beat for thirty minutes after delivery; no autopsy.

DELIVERY FOLLOWING EXTERNAL VERSION

Patient, a gravida vii, with history of five instrumental labors and one still-birth following breech delivery three years previously; five living children; external version at the thirty-sixth week; induction of labor ten days before term; external version repeated at the time of induction of labor; head failed to engage. Axis-traction forceps applied with occiput left and occiput right. Fetus delivered following internal podalic version with forceps to after-coming head.

The irreducible minimum in fetal mortality in my group of 43 cases might have been attained had the two full-term primiparas delivered by breech extraction been permitted to continue longer in the second stage of labor without interference, and the multipara (Grav. vii) subjected to cesarean section.

It would seem that despite congenital absence of one kidney disclosed at autopsy the premature baby of the primiparous patient should have survived, the delivery having been a short, spontaneous one.*

Of the seven fetal deaths two occurred in utero, one following an intrapartum eclamptic convulsion, the other resulting from placental disease several days before the onset of labor. The death of one premature was ascribed to shock accompanying spontaneous labor. Four deaths were due to asphyxia and probable intracranial injury accompanying difficult breech extraction under anesthesia.

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^{*}Of eleven deaths in sixty-eight breech cases delivered in the Sacramento hospitals in 1934 six were prematures of the period of viability. How fetal shock in the premature group may be lessened is a problem which demands serious consideration on the part of the profession.

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WATER CONCENTRATION OF THE BLOOD DURING PREGNANCY, LABOR, AND THE PUERPERIUM*

FRED W. OBERST, PH.D., AND E. D. PLASS, M.D., IOWA CITY, IOWA (From the Department of Obstetrics and Gynecology, State University of Iowa)

T IS generally agreed that pregnancy is associated with a definite blood dilution and with a corresponding increase in total blood volume. It has, moreover, been suggested that these factors may explain the diminished red-cell count and lowered hemoglobin concentration commonly observed during gestation and frequently thought to be clinically significant. This study is concerned with the moisture content of plasma and cells in relation to variations in the plasma proteins and the cell hemoglobin.

Nasse,1 Jones,2 Zangemeister,3 and Polowe4 have observed a decrease in the specific gravity, while the observations of Plass and Bogert,5 and others, on the plasma proteins indicate an increased hydration of the blood plasma with a maximum dilution during the middle of gestation and a subsequent concentration as term is approached. Stander and Tyler6 found that "after the first month, which may be attended with a low plasma moisture, the water increases gradually to the fifth month, after which it falls slowly until the time of labor." Schmidt, Bickenbach, and Jonen have noted an increase in the water content of the blood of dogs during gestation. Direct determinations by various methods, Kaboth,8 Gueissaz and Wanner,9 Miller, Keith, and Rowntree,10 Stander and Creadick,11 Bohnen and Borrmann,12 and Dieckmann and Wegner¹³ have confirmed the indirect evidence pointing toward an increased total blood volume during pregnancy.

SUBJECTS

The subjects of the study included 20 pregnant women (10 primigravidas and 10 multigravidas), 10 parturient women, 10 puerperal women, and 10 nonpregnant women, who served as controls. pregnant women were in the latter part of the third trimester of pregnancy. All of the obstetric patients were chosen from the Maternity Ward of the University Hospitals and were clinically free from

^{*}Presented before the meeting of the American Society of Biological Chemists at Detroit, April 10 to 13, 1935.

disturbing disease conditions, while the nonpregnant group consisted of nurses, and of patients with minor complaints who were on the gynecologic wards. All individuals were given an ordinary mixed diet, and, except for the parturient and puerperal patients, were not confined to bed.

METHODS AND CALCULATIONS

Blood from the adults was obtained some hours after the last meal, except that in the group of parturient women it was drawn at the beginning and again at the end of labor as the occasion demanded. Cord blood was obtained from the children born to mothers who were studied during labor and was aspirated from the umbilical vein before the cord was ligated. All collections were made anaerobically and stasis was avoided. Heparin was employed to prevent coagulation in the portion which was used for the determinations of cell volume, hemoglobin content, specific gravity, and water concentrations, while the remainder was transferred without contact with air to a centrifuge tube containing oil and sodium oxalate. After centrifuging, the plasma was removed for determination of its protein and non-protein nitrogen contents.

Cell volume was determined in Plass and Rourke¹⁴ sedimentation tubes after rotation for thirty minutes at approximately 3,000 r.p.m.

Specific gravity was determined by transferring (blowing out the last drop) 2.0 c.c. of plasma or whole blood from an Ostwald-Folin pipette into a tared 25 c.c. crucible and weighing to the fourth decimal place. After drying the specimen to constant weight in an oven at 105° C., the water content was determined by difference. The specific gravity of the cells was calculated by the formula:

S. G. cells*
$$=$$
 $\frac{100 \text{ (S. G. of W. B.)} - \text{S. G. of Pl.} \times \text{Pl. Vol.}}{\text{Cell volume}}$

*Hg.=Hemoglobin Kg.=Kilogram W.B.=Whole blood S.G.=Specific gravity G.=Grams Pl.=Plasma Vol.=Volume per cent

The water concentration of the cells was calculated by the formula:

$$G.H_2O \text{ per } 100^*$$
c.c. cells $=$ $\frac{100 \text{ (G.H}_2O \text{ per } 100 \text{ c.c. W. B.)} - G.H_2O \text{ per } 100 \text{ c.c. Pl.} \times Pl. Vol.}{Cell \text{ volume}}$

CELL VOLUME RESULTS TABLE I

MATERIAL	CELL VOLU AVERAGE	TME PER CENT* RANGE
Normal nonpregnant women	39.7	34.0-46.5
Late normal pregnancy, primigravidas	36.1	29.2-42.0
Late normal pregnancy, multigravidas	34.6	30.5-37.6
Early in labor	39.3	35.0-44.0
At delivery	41.4	37.2-47.2
Postpartum (7 to 9 days after delivery)	42.7	39.0-53.0
Umbilical cord blood	52.1	42.2-60.2

^{*}In order to conserve space, only maximum and minimum values and averages are recorded in this and subsequent tables.

The water content per kilogram of whole blood, plasma, or cells was obtained by dividing the water per 1,000 c.c. by the approximate specific gravity as determined or calculated.

Hemoglobin concentration was calculated from the oxygen capacity values obtained by the manometric method of Van Slyke and Neill15 and the gas apparatus and technic of Van Slyke. 16 After subtracting 0.5 volume per cent from the observed oxygen capacity to allow for the dissolved or free oxygen, the result was multiplied

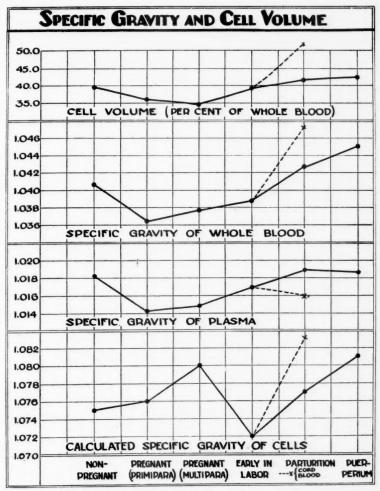


Chart 1.

by the conversion factor, 0.746. (Oxygen capacity in volumes per cent × 0.746 = grams hemoglobin per 100 c.c. blood.) The hemoglobin content per kilogram of cells and per kilogram of water was calculated from the hemoglobin per 100 c.c. whole blood, the cell volume and specific gravity of whole blood, and the water content of the cells by the following formulas:

$$\begin{array}{c} \text{Hg per Kg. cells*} = \frac{\text{G. Hg per 100 c.c. W. B.} \times 1000}{\text{Cell Vol.} \times \text{S. G. cells}} \\ \text{Hg per Kg. H}_2\text{O} = \frac{\text{Hg per Kg. cells} \times 1000}{\text{G. H}_2\text{O per Kg. cells}} \end{array}$$

The total nitrogen of the plasma was determined by the micro-Kjeldahl methodia and the nonprotein nitrogen by the procedure of Folin and Wu, 18 The protein nitrogen as obtained by subtraction was multiplied by the usual conversion factor, 6.25, to obtain the total protein percentage.

By calculations based upon these data it was possible to determine the specific gravity, water content and hemoglobin of the cells, as well as to estimate very closely the distribution of water in a given quantity (1.0 kilogram) of cells and plasma.

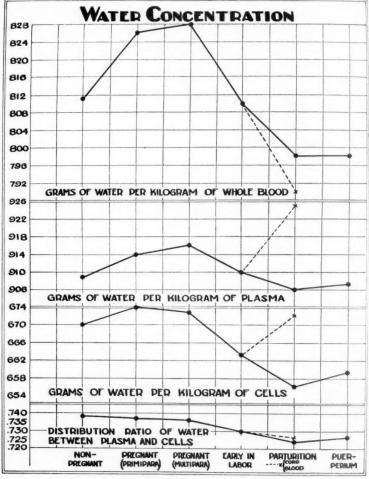


Chart 2.

The average cell volume for the ten normal nonpregnant women (39.7 per cent) (Table I) was slightly below the value given by Osgood and Haskins, 19 41.0 per cent. The diminution of cell volume in late pregnancy is apparent, with the multigravidas exhibiting a greater decrease than the primigravidas. Even at the onset of labor there is a considerable concentration of the blood, which becomes more marked during parturition. The finding of an increased cell volume early in labor may be correlated with the observation first recorded by Zangemeister³ that immediately preceding parturition there is a considerable weight loss, possibly metabolic in origin.

Our observations on puerperal women do not include the first few days after delivery when there is a temporary further dilution of the blood,5 but demonstrate that the normal concentration has been reached by the end of the first week. The table (Table I) also confirms the previously recorded fact that cord blood has a very high cell volume.

Specific Gravity.—It is logical to expect that the specific gravity of the plasma and whole blood will vary with the cell volume since both changes are apparently dependent upon blood dilution.

The specific gravity of whole blood in normal women has been reported by Schmaltz,²⁰ Leake, Kohl, and Stebbins,²¹ and Polowe,²² as averaging 1.053, a value considerably higher than our figure of 1.041. These authors used the Barbour and Hamilton method,23 while the values recorded here were obtained gravimetrically. In spite of this difference, and without questioning the accuracy of either procedure, it is obvious that our values are directly comparable with one another for the purposes of this study.

Thompson²⁴ found that the specific gravity of whole blood in the early months of pregnancy was usually normal or increased, but diminished progressively during the latter months, and rose again nearly to normal at parturition. He related the changes in specific gravity to alterations in the quantity of red cells. Our observations are confirmatory of this finding.

The changes in specific gravity of plasma and whole blood in Table II are consistent with the cell volume variations and associated plasma protein changes, and

	PLASMA	WHOLE BLOOD	RED BLOOD CELLS
Normal nonpregnant women	1.0181 (1.0135-1.0232)	1.0406 $(1.0328 \cdot 1.0473)$	1.075 $(1.053-1.095)$
Late normal pregnancy, primigravidas	$\substack{1.0152 \\ (1.0095 \cdot 1.0195)}$	1.0363 (1.0300-1.0409)	1.076 (1.063-1.084)
Late normal pregnancy, multigravidas	$\substack{1.0155 \\ (1.0101 \cdot 1.0206)}$	1.0376 (1.0335-1.0409)	1.080 $(1.070-1.099)$
Early in labor	$\substack{1.0168 \\ (1.0123 \cdot 1.0211)}$	1.0387 $(1.0337 \cdot 1.0465)$	1.072 $(1.053-1.091)$
At delivery	$\substack{1.0189 \\ (1.0159 \cdot 1.0250)}$	$\substack{1.0425 \\ (1.0374 \text{-} 1.0470)}$	1.077 $(1.052-1.090)$
Postpartum 7-9 days after delivery	$\substack{1.0186 \\ (1.0153 \cdot 1.0212)}$	$\substack{1.0450 \\ (1.0391 \cdot 1.0505)}$	1.081 $(1.071-1.090)$
Umbilical cord blood	1.0159 $(1.0127-1.0202)$	1.0472 (1.0403-1.0515)	1.083 $(1.075-1.099)$

TABLE II. SPECIFIC GRAVITIES

point to dilution as a common etiologic factor, whereas the changes in specific gravity of the cells are possibly within the limits of experimental error.

Polowe4 suggested that a whole blood specific gravity (Barbour-Hamilton method) below 1.050 represented a definite anemia, and, employing this standard, noted an anemia in 66 per cent of his patients in the first, 70 per cent in the second, and 83 per cent in the third trimester of gestation. During the seventh lunar month, every patient presented a specific gravity of less than 1.050. In the puerperium, 85 per cent of his patients presented an anemia, which tended to be more marked than during pregnancy.

Our findings confirm the diminution of the specific gravity of the whole blood late in gestation, but the average hemoglobin values do not indicate a significant anemia. The specific gravity of whole blood does not vary mathematically with the hemoglobin content.

Water Content.—The water content of the plasma and whole blood was determined and that of the blood cells calculated to give the data in Table III.

The changes in water content follow those of specific gravity but are in the reverse direction, while the distribution ratio between cells and plasma

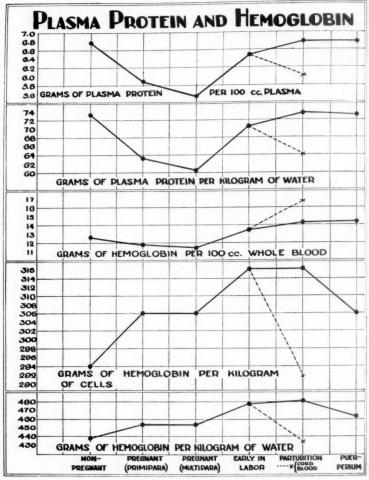


Chart 3.

 $\left(\frac{\text{Water per Kg. of cells}}{\text{Water per Kg. of plasma}}\right)$ is quite constant, the average being 0.731 and the range 0.724 to 0.738. These alterations may be explained by dilution, and it would seem that variations in the water content of the plasma affect the suspended cells directly, since the distribution ratio remains so nearly constant.

Hemoglobin values for normal nonpregnant women are again slightly below the average determined by Osgood and Haskins¹⁹ on 100 normal women, namely 13.69 (10.98 to 16.49) gm. of hemoglobin per 100 c.c. blood. While our lower values (Table IV) may indicate a mild unrecognized anemia in certain members of the group, the discrepancy is not material. During pregnancy the hemoglobin percentage

falls considerably, to rise abruptly at labor and is at this new high point during the early part of the second week of the puerperium, while the hemoglobin per 1,000 gm, of cells increases as the hemoglobin of the whole blood falls. During labor both factors rise. In the second week following delivery the whole blood hemoglobin

TABLE III. WATER (IN GRAMS) PER KILOGRAM

	PLASMA	WHOLE BLOOD	RED BLOOD CELLS
Normal nonpregnant women	909 (895-922)	811 (799-828)	670 (657-679)
Late normal pregnancy, primigravidas	914 $(907-920)$	$826 \ (806-845)$	$674 \\ (651-684)$
Late normal pregnancy, multigravidas	915 (908-922)	828 (819-839)	673 (662-688)
Early in labor	910 (903-914)	809 (798-823)	$663 \ (658-682)$
At delivery	906 (898-914)	798 (786-815)	$656 \ (647-666)$
Postpartum (7-9 days after delivery)	907 (899-916)	798 (769-813)	659 (645-679)
Umbilical cord blood	925 (912-928)	$791 \ (766-812)$	$672 \\ (664-684)$

TABLE IV. HEMOGLOBIN

	GRAMS PER 100 C.C. WHOLE BLOOD	GRAMS PER 1000 GRAM CELLS	GRAMS PER 1000 GRAMS WATER
Normal nonpregnant	12.53 (10.83-14.32)	294 (285-310)	438 (399-468)
Late normal pregnancy, primigravidas	$11.93 \\ (9.25 \cdot 14.02)$	$306 \\ (287-337)$	455 $(426-498)$
Late normal pregnancy, multigravidas	11.45 $(10.37-12.90)$	$306 \ (252-349)$	$455 \\ (416-549)$
Early in labor	$13.36 \\ (11.92 \cdot 14.94)$	316 (290-338)	477 $(441-510)$
At delivery	$14.10 \\ (12.90 \cdot 16.04)$	316 $(300-330)$	481 $(462-510)$
Postpartum (7-9 days after delivery)	$14.13 \\ (12.35 \cdot 17.01)$	$306 \ (288-352)$	$464 \ (425.546)$
Umbilical cord blood	16.50 $(15.30-18.88)$	$292 \ (260-331)$	435 (388-498)

is still elevated although the concentration of hemoglobin in the cells has fallen below the pregnancy level. The curve of the hemoglobin per 1,000 gm. of water in the red cells follows that of the hemoglobin per unit mass of cells.

Plasma Proteins .- The concentration of plasma proteins varies directly with the plasma water content (Table V). During late pregnancy, there is a decreased protein concentration, but in the early part of labor the protein percentage is increased and rises still higher as delivery is approached. This curve is the reverse of that obtaining for the water content of the plasma, a fact which emphasizes the

direct relation which dilution has upon the protein concentration. The average values for grams of protein per 1,000 gm. of water in the plasma are roughly parallel to the plasma protein percentages, thus confirming still further the opinion that pregnancy is associated with plasma dilution. The protein content of cord blood is consistently lower than that of maternal blood.

TABLE V. PLASMA PROTEINS

	GRAMS PER 100 C.C.	GRAMS PER 1000 GRAMS OF WATER
Normal nonpregnant	6.77 (5.93-7.79)	73.4
Late normal pregnancy, primigravidas	5.89 $(5.06-7.28)$	63.5
Late normal pregnancy, multigravidas	5.61 $(5.01-7.27)$	60.4
Early in labor	6.51 $(5.93-6.93)$	70.4
At delivery	6.77 (6.41-7.09)	73.6
Postpartum (7-9 days after delivery)	$6.73 \\ (6.23-7.61)$	72.9
Umbilical cord blood	6.00 (5.34-6.72)	63.9

DISCUSSION

The observations here recorded confirm existing evidence of consistent variations in the specific gravity and cell volume of the whole blood during pregnancy, labor and the early puerperium, and relate these changes more definitely to dilution by emphasizing the determined variations in water concentration of the various fractions of the blood.

The water concentration of the whole blood is significantly increased during gestation, but falls to a normal level as parturition is approached and drops below normal at the time of delivery. One week after delivery there is no demonstrable change from normal. The water concentrations in the plasma and cells follow a similar curve.

While these changes are producing a blood dilution, the constitution of the cells is being altered. The hemoglobin content of cells (grams per kilogram) is increased in the latter part of gestation and further increased during labor, when it is approximately 7 per cent higher than in nonpregnant women. After delivery there is a slight decrease. With the water concentration of the cells rising slightly during gestation, it may be assumed that the corresponding increase in hemoglobin represents an actual new production. The parturitional changes are evidently comparable to those which have been described by Dill, Talbott, and Edwards²⁵ as occurring during muscular activity, and are probably due to the dehydration which apparently affects all portions of the circulating blood. The ratio of distribution of water

between the cells and the plasma is remarkably constant but is lowered to a certain extent during labor, thus indicating a tendency toward the replacement of water taken from the plasma by that available in the cells. We have no adequate explanation for the observed lowering of cell specific gravity during labor, when the decrease in water and increase of hemoglobin in the cells would seemingly operate in the opposite direction, unless the leucocytosis commonly present at that time may be sufficient to produce the change, the white blood cells being considerably lighter than the red cells.

It is interesting that the hemoglobin content of the whole blood during the second week after delivery is the same as at the time of labor, in spite of the physiologic loss of blood during this interval. The water concentration of the whole blood and plasma does not change, but there is a slight rise in the cell volume and a decrease in the hemoglobin per kilogram of cells, which apparently are directly compensatory.

These observations present additional confirmation of the opinion that the mild gestational anemia consistently determined by clinical methods is more apparent than real, the entire phenomenon being dependent upon a marked dilution which affects both the plasma and the cells. It should also be pointed out that the subcutaneous edema present in the majority of pregnant women introduces an error into clinical determinations made upon finger-prick blood. Unpublished observations in this laboratory indicate that a very significant reduction of hemoglobin content and red cell count can be explained in this fashion.

SUMMARY

During the active childbearing function of women, the water concentrations of whole blood, plasma, and cells follow the same general curve, which is the reverse of that noted for specific gravity of whole blood and plasma, cell volume, plasma proteins, and hemoglobin content of whole blood. These findings confirm the conception of a blood dilution during pregnancy with prompt elimination of the excess water during parturition and the puerperium.

There is evidence that the body attempts to compensate for this dilution by increasing the hemoglobin content of individual cells, which consequently show an increased specific gravity.

The slight anemia of normally pregnant women recognized by clinical methods is only apparent and can be explained by physiologic dilution of the blood associated with an increased blood volume, and by the further dilution of finger-prick blood with the fluid from edematous subcutaneous tissues.

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PNEUMOCOCCUS PELVIC INFECTION IN WOMEN

PENDLETON TOMPKINS, M.D., PHILADELPHIA, PA.

(From the Gynecean Hospital Institute of Gynecologic Research and the Department of Gynecology of the Hospital of the University of Pennsylvania.)

S INCE the publications of Michaut¹ and Jensen² thirty-five years ago, pediatricians and general surgeons have been familiar with the pneumococcus as a cause of peritonitis, but only recently has the attention of obstetricians and gynecologists been directed to this organism as a cause of puerperal infection and chronic pelvic inflammatory disease. King,3 who recently reported three cases of pneumococcus pelvic infection from his own experience and collected eleven cases from the literature, believes that pneumococcus infection is more frequent in obstetrics and gynecology than these few reports indicate. This seems probable, for at the Hospital of the University of Pennsylvania three cases of localized pneumococcus pelvic inflammatory disease were observed in the Department of Gynecology in the course of a single year. These three cases occurred among approximately 1,000 gynecologic patients who were admitted to the hospital between Sept. 1, 1933, and Sept. 1, 1934. No special search for pneumococci was being made at the time, and there was no unusual respiratory epidemic in progress. The report of these three cases is preceded by a discussion of pneumococcus pelvic infection, and by a tabulation of twenty-four similar reports found in a search of the literature.

TABLE I. PNEUMOCOCCUS INFECTION IN OBSTETRICS AND GYNECOLOGY, SUMMARY OF 24 CASES REPORTED IN THE LITERATURE

AUTHOR	REFERENCE	CLINICAL TYPE OF INFECTION	OUTCOME
Elkin	Arch. Surg. 18: 745, 1929	Peritonitis during pregnancy	Death
Hartemann and Lacourt	Bull. Soc. d'Obst. et de gynéc. 23: 451, 1934	Peritonitis during pregnancy	Death
Apert	Bull. et mém. Soc. méd. d. hôp. de Paris 54: 1877, 1930	Puerperal infection	Recovery
Baetjer	Trans. Assn. Am. Physiol. Philadelphia 40: 437, 1925	Puerperal infection	Recovery
Darré, Laederich, and Mamou	Bull. et mém. Soc. méd. d. hôp. de Paris 54 : 1738, 1930	Puerperal infection	Recovery
de la Marnière	Bull. et mém. Soc. nat. de chir. 59: 7, 1933	Puerperal infection	Recovery
Seymour	Brit. M. J. 1: 895, 1928	Puerperal infection	Recovery
Armitage	Brit. M. J. 2: 1185, 1927	Puerperal infection	Death
Baetjer	Loc. cit.	Puerperal infection	Death
Laffont and Ezes	Bull. Soc. d'obst. et de gynée. 21: 543, 1932	Puerperal infection	Death
McCord	AM. J. OBST. & GYNEC. 16:		
McCord	272, 1928	Puerperal infection	Death
MeCora Monckeberg	Loc. cit.	Puerperal infection	Death
Wetzel	Gynéc. et obst. 6: 274, 1922	Puerperal infection	Death
Wetzei	München, med. Wehnschr. 62: 109, 1915	Puerperal infection	Death
Fricke	Am. J. Surg. 3, 48, 1930	Postabortal infec- tion	Recovery
Wolfsohn	Zentralbl. f. C. r. 57: 2842, 1930	Postabortal infec- tion	Recovery
Wolfsohn	Loc. cit.	Postabortal infec- tion	Death
Cole	Nelson's Loose-Leaf Living Medicine 1: 245, 1920	Pelvic abscess	Recovery
Von Rosthorn	Zentralbl. f. Gynäk. 18: 1150, 1894	Pelvic abscess	Recovery
King	Am. J. Obst. & Gynec. 29: 341, 1935	Pelvic abscess	Recovery
King	Loc. cit.	Pelvic abscess	Recovery
King	Loc. cit.	Pelvic abscess	Not stated
Fricke	Loc. cit.	Pyosalpinx	Not stated
Zweifel	Arch. f. Gynäk. 39: 353, 1891	Pyosalpinx	Recovery

ETIOLOGY

Bacteriologic studies have shown that pneumococci may be recovered from the nasopharynx of almost all normal, healthy persons.^{4, 5} It, therefore, seems probable that the respiratory tract is the ultimate source of pneumococci which produce pelvic disease, but the route by which these organisms reach the peritoneal cavity is often a matter of conjecture. The two most likely possibilities are, first, metastatic infection through the blood or lymph from an active focus of pneumococci elsewhere, and second, ascending infection through the female genital tract. The introduction of pneumococci into the abdomi-

nal cavity by trauma is very rare. In animals it has not been possible to demonstrate conclusively that pneumococci can pass directly from the lumen of the intestine into the abdominal cavity, nor has it been possible to produce pneumococcus peritonitis by infection of the blood stream. However, from the clinical standpoint, secondary, or metastatic pneumococcus peritonitis does occur, as a complication not only of pneumonia, but also of other pneumococcus infections such as otitis media or mastoiditis. Many such cases are reported in the male where there is no possibility of ascending infection of the peritoneum.

After reading the publications of McCartney and Fraser^{6, 7} it is reasonable to believe that the pneumococcus can ascend through the female genital tract and cause peritonitis. This view is supported not only by experimental work but also by such clinical evidence as the following:

Monckebergs describes a patient who developed a puerperal infection three days after a normal delivery. The lochia showed a pure culture of pneumococci and the blood culture was positive for this organism. Autopsy showed pneumococcus endometritis, peritonitis, and pneumonia. No pneumococci had been found in the patient's sputum, but they were present in the sputum of the midwife in attendance.

Lambert⁹ reports an extraordinary sequence of cases. The young daughter of a man with pneumonia developed pneumococcus peritoritis. Later she developed pneumonia also. The nurse in attendance upon this girl developed pneumococcus peritoritis, and finally pneumonia.

Reports such as these, while not conclusive evidence of the path of infection, are significant. Generally speaking, unless there is a clear history to the contrary, obstetricians and gynecologists will not be far wrong in assuming that cases of pneumococcus pelvic disease which they see are the result of ascending infection. Pneumococcus peritonitis occurring as a complication of active pneumococcus infection elsewhere in the body is usually generalized, and is usually seen and treated by the general surgeon rather than by the gynecologist.

CLASSIFICATION

Intraabdominal pneumococcus infection may be classified according to the path of infection, the age distribution, or the clinical characteristics.

Since Michaut's description it has been customary to speak of primary and secondary pneumococcus peritonitis. McCartney rigidly defines primary infections as those in which no focus of pneumococcus infection can be demonstrated outside the abdomen. He thereby implies that primary pneumococcus peritonitis cannot be a metastatic, but must be an ascending infection, and that consequently it can occur only in the female. Nevertheless, so-called primary cases are reported in males. The authors of such reports usually state that

no extraabdominal pneumococcus infection was found. However, it is always possible that further search, including cultures of the mastoid cavities and the nasal sinuses, might have revealed a hidden focus of pneumococci. As might be expected, secondary pneumococcus peritonitis occurs with approximately equal frequency in both sexes. The primary or ascending infection is of chief interest to obstetricians and gynecologists.

In obstetrics and gynecology three varieties of pneumococcus infection may be seen: first, acute puerperal or postabortal pelvic infection; second, localized pelvic abscess; third, and least frequently because it is not strictly a gynecologic problem, generalized peritonitis.

INCIDENCE

The literature indicates that pneumococcus peritonitis is perhaps ten times as frequent in children as in adults and that girls are affected from three to seven times as frequently as boys. It has been estimated that 25 per cent or more of all generalized peritonitis in children is due to the pneumococcus. Much less frequently is it the cause of peritonitis in adults. Pflaum determined the causative organism in ninety-seven fatal cases of peritonitis. Only two were due to the pneumococcus; one case followed pneumonia. Pneumonia is complicated by pneumococcus peritonitis in approximately 1 per cent of cases. 12, 13

Bacteriologic studies of fallopian tubes rarely reveal the pneumo-coccus,¹⁴ probably because it tends to produce a generalized peritonitis rather than to remain localized.

The incidence of pneumococcus infection in obstetrics and gynecology cannot be estimated from the data available. Inasmuch as there are no distinguishing clinical characteristics and diagnosis is entirely dependent upon bacteriologic study, it is probable that many cases escape recognition.

SIGNS AND SYMPTOMS

Neither pneumococcus puerperal infection nor localized pneumococcus pelvic inflammatory disease differs sufficiently from similar infections by other organisms to permit a bedside diagnosis. King stresses the importance of a history of recent respiratory infection and reports a case of pneumococcus pelvic infection correctly diagnosed from the history. The association should be kept in mind, but it would be rash to suspect every patient with pelvic inflammatory disease of having pneumococcus infection on the basis of a recent cold.

The signs and symptoms of pneumococcus peritonitis are occasionally sufficiently characteristic to permit a clinical diagnosis before bacteriologic studies have been reported. The disease usually begins

with a slight chill, sudden, severe, cramping lower abdominal pain, diarrhea (green stools), and vomiting. High fever (40° C.), high leucocytosis (30,000) with high polymorphonuclear count (95 per cent), and rapid pulse soon follow. Herpes labialis may be noted. Abdominal rigidity is often not marked. Abdominal distention and constipation appear and are frequently accompanied by bulging in the culdesac, for pneumococci rapidly produce large quantities of pus. Such pneumococcus infection will more often come to the attention of the general surgeon than of the gynecologist.

DIAGNOSIS

In its early stages primary pneumococcus peritonitis is likely to be mistaken for enteritis, salpingitis, or for some acute surgical condition such as appendicitis, pancreatitis, et cetera. Sympson describes a case mistaken for acute oophoritis because it developed during the course of mumps. 15 Although laparotomy is no longer the treatment of choice, the fear of overlooking some operable condition leads most surgeons to operate even when the possibility of pneumococcus peritonitis is borne in mind. Material for bacteriologic examination may be secured by vaginal or abdominal puncture16 but is usually not available prior to laparotomy. Typical pneumococcus pus is profuse, thick, and odorless, and contains the organism in pure culture. In most cases the nature of the infection is realized before the results of blood culture can be reported, so this procedure is of confirmatory and prognostic rather than of diagnostic value. Bacteriologic examination of the lower genital tract may be helpful. Since the pneumococcus is almost never present in the normal vaginal discharges, its discovery in cervical or uterine secretions is of considerable significance. In all cases the diagnosis ultimately depends upon the bacteriologist; when pneumococci are found they should be typed in anticipation of the use of specific antipneumococcus serum.

PROGNOSIS

The prognosis of localized pneumococcus pelvic infections such as culdesac abscesses that can be drained, or tuboovarian abscesses that can be removed en masse, is good, but in other pneumococcus intra-abdominal infection the outlook is grave. Pneumonia, which is not an infrequent sequel, is more apt to develop if inhalation anesthesia has been administered.

TREATMENT

The present trend in the treatment of generalized pneumococcus peritonitis is away from laparotomy and toward conservative measures in hope that localization will occur. In actual practice, however, since the diagnosis is usually not definitely established prior to operation, most patients are submitted to laparotomy and drainage.

A number of "specific" remedies have been suggested such as optochin, solutions of bile salts, autogenous vaccines, and antipneumococcus serum. Since no special treatment has been employed often enough to permit its evaluation, the management of pneumococcus pelvic infection, whether localized, puerperal, or postabortal, does not differ at present from that of similar infections of different etiology.

Antipneumococcus serum should have further trial not only because it may favorably affect the abdominal disease but also because it may decrease the patient's liability to pneumococcus pneumonia. It has been used for instillation into drainage tubes as well as for the usual intravenous injection. The type of serum used should match the type of pneumococcus found.

PROPHYLAXIS

Prophylaxis against ascending pneumococcus infection of the abdominal cavity consists in preventing pneumococcus infection of the lower genital tract. How such infection occurs can only be surmised. It is believed that scantily clad girls who sit in unclean places may be infected by direct contact, that pneumococci may be transferred from the respiratory passages by the hands, and that obstetric patients may be infected by respiratory droplets during labor and delivery. Condoms lubricated with saliva, a practice not uncommon among the lower classes, may also be a source of infection. Other possibilities suggest themselves.

It is remarkable that an organism such as the pneumococcus which is constantly found in the respiratory passages and which has an affinity for mucous surfaces should so seldom be found in the vagina. Perhaps, as the investigations of Schutt¹⁷ indicate, it is destroyed by the normal acid vaginal discharges. Schutt's studies may provide a clue to the susceptibility of children to ascending pneumococcus infection, since their vaginal discharges are less acid than those of the adult.

When a case of pneumococcus puerperal infection is recognized, an attempt should be made to discover its source. Cultures for pneumococci should be taken from the nasopharynx of the patient, and if these are negative, cultures should be taken from the attending staff. Investigations of this type, by disclosing the probable source of pneumococcus puerperal infection, will contribute to its prevention.

REPORT OF CASES

Case 1.—Pelvic abscess, pneumococcus Type I, colpotomy, recovery. Mrs. M. P. (Gyn. No. 23390½), aged thirty-seven, married eighteen years, para vii, was admitted to the Hospital of the University of Pennsylvania on Dec. 26, 1933. Her remote

history included mumps in childhood and an appendectomy in 1913. The patient had never had pneumonia. Her last child was born in August, 1933; the delivery and puerperium had been uneventful. Menstruation had been normal prior to this pregnancy but had not occurred since. On December 13, four months after delivery, while in apparent good health, the patient had a sudden attack of cramping bilateral lower abdominal pain with nausea and vomiting. Shortly thereafter a watery mucoid diarrhea developed. Night sweats occurred and were accompanied by fever which on one occasion reached 102° F. The patient became rapidly weaker and stated that her weight had decreased from 115 pounds to 88 pounds in two weeks. Profuse leucorrhea developed. Two weeks after the onset of symptoms she entered the Gynecologic Ward. The patient denied any recent respiratory infection.

General physical examination was negative except that the patient was obviously in poor physical condition and had lost weight. The chest was clear. Pelvic examination revealed a cyst of the left vulvovaginal gland and a fluctuating adnexal mass pushing the uterus to the right. Diagnosis: left tubovarian abscess.

Laboratory Report: 4.8 million erythrocytes and 12,800 leucocytes (90 per cent polymorphonuclears) per c. mm. of blood. Blood Wassermann and urinalysis negative. The erythrocyte sedimentation rate based on a normal settling of 23 mm. in two hours or more, was fast (thirty-five minutes).

On December 27 a colpotomy was performed by Dr. Charles Behney under local anesthesia. About 200 c.c. of thick pus was released and a drain was inserted. The pus showed a pure culture of Type I pneumococcus. Blood culture, taken Jan. 2, 1934, was negative. On January 3 the sedimentation rate was sixty minutes. The patient was discharged to a convalescent home on January 10, much improved.

Follow-up examination, January 24, showed continued improvement. The patient was last examined May 2, 1934. No adnexal masses were palpable. She had gained 20 pounds.

Case 2.—Tubovarian abscess, pneumococcus Type IV, laparotomy, recovery. Mrs. M. W. (Gyn. No. 23221), aged forty-two, married twenty-one years, completed a normal pregnancy and delivery in 1914. Gonorrheal infection in 1915 was followed by ankylosis of the right wrist. There were no subsequent pregnancies. In 1915 the cervix was amputated and a colporrhaphy was performed. Excepting for mumps in childhood the history was negative. The patient had never had pneumonia. On October 21, 1933, while in apparent good health, the patient developed bilateral lower abdominal pain and fever. There was no nausea, vomiting, or diarrhea. The patient was not prostrated, but continued to work as a clerk. On October 27, three days before the expected date, menstruation began with dysmenorrhea and passage of clots, symptoms never previously noted. A few days later thick leucorrhea appeared. This was accompanied by fever which at times reached 101° F. On Nov. 6, 1933, the patient entered the Gynecologic Ward. She denied any recent respiratory infection.

General physical examination was negative. The chest was clear. Pelvic examination revealed bilateral, fixed, tender adnexal masses which extended 6 cm. above the level of the symphysis. Diagnosis: pelvic inflammatory disease.

Laboratory Report: 3.8 million erythrocytes and 27,500 leucocytes per c. mm. of blood. Blood Wassermann and urinalysis negative. Sedimentation rate fifteen minutes (two hours taken as normal).

After two weeks of conservative treatment there was little improvement. On November 17 the sedimentation rate was seventeen minutes. On November 19 the patient returned home to continue conservative treatment. She improved gradually and resumed her work as a clerk. On Jan. 26, 1934, after recurrence of abdominal pain, the patient reentered the hospital. At this time the pelvic induration was

more localized, the leucocyte count was 15,500 per c. mm. of blood, and the sedimentation time was twenty-one minutes.

On January 27 a laparotomy was performed by Dr. Robert Kimbrough under nitrous oxide and ether anesthesia, and approximately one liter of green pus was evacuated from a right tubovarian abscess. Drains were inserted and the abdomen was closed. Culture of the pus showed pneumococcus, Type IV, and a few hemolytic streptococci. The patient's recovery was uneventful.

Follow-up examination in August, 1934, disclosed a right adnexal mass about 6 cm. in diameter. The patient was in good health, had no complaints, and had gained a few pounds. The sedimentation rate was still rapid (seventy minutes).

Case 3.—Tubovarian abscess, pneumococcus Type III, laparotomy, prolonged recovery. Mrs. R. D. (Gyn. No. 23332), aged thirty-three, married eighteen years, para ii, completed her last pregnancy in 1918. The puerperium was normal. She had had pneumonia in 1917 and a right salpingo-oophorectomy and appendectomy in 1925. No bacteriologic studies were made at the time of this operation. Her present illness began during 1932 with occasional dull pain in the left lower abdominal quadrant. In August, 1933, "inflammation of the bladder" developed with dysuria, urinary frequency, pain in the left lower quadrant and fever of 103° F. At this time profuse leucorrhea appeared. After two weeks in bed at home there was some improvement but the abdominal pain continued. The patient entered the Gynecologic Ward Dec. 5, 1933, complaining of pain in the left lower abdomen, leucorrhea, dysuria, and loss of 27 pounds in the preceding four months.

General physical examination was negative. The chest was clear. Pelvic examination revealed a tender nodular mass about 8 cm. in diameter adherent to and anterior to the retroflexed uterus. Diagnosis: pelvic inflammatory disease, possibly a tuboovarian abscess.

Laboratory Report: 4.4 million erythrocytes and 15,600 leucocytes per c. mm. of blood. Blood Wassermann and urinalysis negative. Sedimentation rate twenty-six minutes (two hours regarded as normal).

Conservative treatment was instituted, but after four weeks the patient made no improvement so, on Jan. 6, 1934, Dr. Floyd Keene performed a laparotomy which revealed a densely adherent left tuboovarian abscess. The patient's condition on the table was so poor that the difficult salpingo-oophorectomy was not attempted. Several ounces of thick, greenish pus were evacuated. Drains were inserted. Culture of the pus showed a pure growth of Type III pneumococcus.

Recovery was slow. On Jan. 27, 1934, the patient left the hospital. Her wound continued to drain. She was examined every three months during the next year. During this time the draining sinus did not heal, nor did the pelvic mass decrease in size. The sedimentation rate remained rapid (thirty minutes).

The patient reentered the hospital Jan. 27, 1935, and 300 c.c. of serous fluid was removed by vaginal puncture. Culture of the pus from the abdominal sinus still showed pneumococci. Efforts to improve the patient's general condition were unsuccessful and she returned home.

At follow-up examination May 29, 1935, the sinus was still draining and the pelvic mass extended almost to the umbilicus. However, the patient had gained 20 pounds, had no pain, and felt much improved. The sedimentation rate was forty-five minutes.

SUMMARY

Pneumococcus pelvic infection has been presented as an unusual problem in obstetrics and gynecology. The incidence, origin, diag-

nosis, prognosis, and treatment of such infection have been discussed and measures for clinical study and for prophylaxis have been suggested. Twenty-four cases have been cited from the literature and three new cases have been reported in detail.

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A STUDY OF THE BLOOD LOSS IN THE THIRD STAGE OF LABOR AND THE FACTORS INVOLVED

JOHN B. PASTORE, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Cornell University Medical College and the New York Hospital)

IN A RECENT issue of the American Journal of Obstetrics and Gynecology, 10 I described a new method of measuring the blood loss during the third stage of labor. This method has been used routinely in the Woman's Clinic of the New York Hospital since September, 1934.

Shortly after the institution of this routine we were impressed by the increase in the incidence of postpartum hemorrhage. The question immediately arose as to whether it was due to mismanagement of the third stage or to the fact that the blood loss was measured. For this reason a study was made of the deliveries during September, 1933, and the corresponding month in 1934. The results are shown in Fig. 1 and Table I. All of the cases measured in the 1933 series were in the hemorrhage group.

TABLE I. COMPARISON OF MEASURED AND ESTIMATED BLOOD LOSSES

	1			AVERAGE BLOOD LOSS	HEMORRHAGES		
	CASES	MEASURED	ESTIMATED		CASES	PER CENT	AVERAGE BLOOD LOSS
September 1933	197	3.5%	96.5%	252.4 e.e.	7	3.55	1228 c.e.
September 1934	177	80.0	20.0	264.3 c.c.	16	9.05	806 c.c.

Over 67 per cent of the cases in the 1933 series were estimated in groups of 100 c.c. and 200 c.c. of blood loss. Although there is an increase in postpartum hemorrhage from 3.55 per cent to 9.05 per cent in the measured group, one notes an increase from 4.5 per cent to 19.2 per cent in the losses less than 100 c.c. The average blood loss in each series was practically the same. One can conclude, therefore, that there is a tendency to underestimate losses above 450 c.c. and to overestimate losses below 150 c.c.

The graph in Fig. 1 also shows the fallacy of trying to compare reports on postpartum hemorrhages, unless the percentage in each 100 e.c. blood loss group is given in addition to the average blood loss and the incidence of hemorrhage. In the 1933 series there were four cases

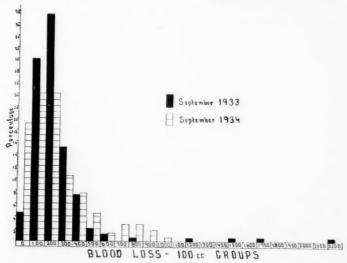


Fig. 1.—Comparison of estimated and measured blood losses. 1933 estimated; 1934 measured.

of hemorrhage of more than 1,000 c.c. in spite of the fact that the incidence was almost one-third of that in 1934. These patients were obviously in a more critical and serious condition than any of the patients in the 1934 series, whose maximum blood loss was in the 1,000 c.c. group. This statement is corroborated by the fact that the average blood loss in the hemorrhage group of each series was 1,228 c.c. in 1933 and 806 c.c. in 1934.

THE PRESENT STUDY

The present study includes 574 consecutive vaginal deliveries of full-term or premature babies. Of these cases 74 were either incompletely measured or estimated, as some of the deliveries were conducted on the Isolation Floor, and are, therefore, not included in the analytical study. The incidence of hemorrhage in this estimated

group was 5.4 per cent. At the present time it is possible to measure accurately over 95 per cent of the cases delivered. Most of the deliveries were conducted by the house staff or the fourth-year medical students. The more difficult operative procedures were carried out by the Resident on Obstetrics under the supervision of the attending staff, or by the attending surgeon. Both spontaneous and operative vaginal deliveries are included in the study.

In the 500 consecutive cases there were 32 cases in which the blood loss was 600 c.c. or more, giving an incidence of 6.4 per cent. There were no maternal mortalities. This is considerably less than the 13 per cent incidence reported by Williams in his series of 1,000 consecutive spontaneous deliveries. Polak in 1915 reported 1,306 consecutive home deliveries without a hemorrhage and 694 operative deliveries with

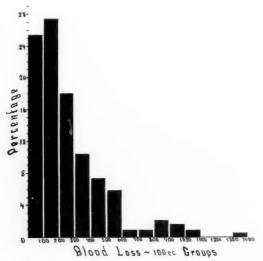


Fig. 2.—Distribution of blood losses in 100 c.c. groups: 0 to 99 c.c., 100 to 199 c.c., etc.

only three hemorrhages. Brandt in 1933 reported only 10 hemorrhages in 800 consecutive deliveries. Both of these reports are based on estimation of the blood loss in contrast to Williams' accurate measurements in his series. The largest series reported is that of Peckham and Kuder in a study of 19,200 consecutive deliveries at the Johns Hopkins Hospital. They found an incidence of 6.14 per cent but neglected to state the percentage of cases in which the blood loss was measured. Calkins reported in 1933 an incidence of 2.5 per cent in 800 cases. However, the blood loss in these cases is only partially measured by the Calkins technic.

The average blood loss in our series was 244.3 c.c. in contrast to Williams' 343.7 c.c. (measured), Ahlfeld's 505.1 c.c. (measured), Tucker's 300 c.c. (measured), Calkins' 222 c.c. and 179 c.c. (partially measured), and Brandt's 6½ ounces. It is difficult to compare these figures because of lack of standardization in the methods used. The difference in figures reported by Ahlfeld and Williams may be accounted for by their different method of management of the third stage. In our own series we have employed Calkins' modification of the Williams technic in determining the separation of the placenta.

In Fig. 2 the distribution of the blood loss is represented. Seventy and four-tenths per cent of the patients had a loss of less than 300 c.c. Calkins reported 89 per cent of

the losses to be less than 300 c.c. There were two patients who had losses in the 1,300 c.c. group. Since the opening of the Woman's Clinic in September, 1932, there have been eighteen patients in whom the blood loss was 1,500 c.c. or more, five of these occurring in 1934 prior to our present method of measuring the blood loss. The largest blood loss which we have had in approximately 1,400 deliveries since September, 1934, has been in the 1,300 c.c. group. This I think is due to the fact that with the use of the apparatus the operator is constantly aware of the blood loss and is therefore in a position to manage the third stage more efficiently. The incidence of shock has been markedly reduced during the past seven months, and we have had no patient who was thought to be in a critical condition because of the blood loss.

In 1919 Williams was impressed by the tolerance of recently delivered women to excessive blood loss. He offered as an explanation for

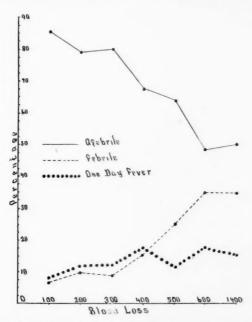


Fig. 3.—Puerperium in relation to blood loss. First group 0 to 99 c.c., second 100 to 199 c.c., etc. Last figure is for the hemorrhage group.

this the increase in blood volume and the development of some protective mechanism during pregnancy and labor. It seemed necessary, therefore, in this study to study not only the immediate reaction to hemorrhage but also the patient's course during the puerperium. Fig. 3 shows graphically the relation of the puerperium to the blood loss. There is a definite increase in morbidity with increase in blood loss. In our classification all patients who have a rise in temperature to 38° C. or more on two occasions for over twenty-four hours and excluding the first twenty-four hours after delivery are considered febrile. This increase is directly due to puerperal infection, since it accounted for 69.64 per cent of the febrile cases without hemorrhage,

and 90.90 per cent of those with hemorrhage. Obviously, although the recently delivered patient has tolerance to the immediate dangers of hemorrhage, yet her tolerance or resistance to infection is decreased. Fig. 4 shows that the average stay in the hospital after delivery increases with the blood loss. In both of these charts all the hemorrhages are grouped together in the last figure. Our attention, therefore, should be directed toward decreasing not only the incidence of hemorrhage but also the average blood loss, as pointed out by Calkins.

The various factors involved throughout pregnancy will be presented separately.

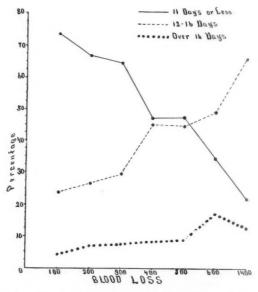


Fig. 4.—Postpartum days in hospital in relation to blood loss. Same scale as in Fig. 3.

Influence of the Age of the Patient.—Table II shows the incidence of hemorrhage and the average blood loss in four age groups. Contrary to the findings of Calkins and Peckham and Kuder, age seems to have a direct effect on the blood loss, as was first shown by Ahlfeld.

Race.—There were only twenty-six colored patients in our series so that no definite conclusions can be drawn. Of these 7.6 per cent had blood losses in excess of 600 c.c.

Complications of Pregnancy.—The thirteen cases of cardiac disease in this series showed a slight increase in blood loss, with an incidence of hemorrhage of 7.70 per cent and an average blood loss of 280 c.c. Some of this increase may be explained by the fact that the severe cardiacs receive drop ether anesthesia during the second stage of labor, and also the operative incidence is higher. Contrary to our expectations myomas of the uterus caused no appreciable increase. Only one of the sixteen patients had excessive blood loss, and this patient lost 900 c.c. The uterus was packed because of continued bleeding in spite of the fact that the uterus was firm. The average blood loss for the group was 256 c.c. No definite differentiation as to the type of the myoma could be made, and it is quite probable that in our series most of these were subserous.

No conclusion can be drawn from the cases of antepartum bleeding as the severe cases of separation of the placenta and the central placenta previas were treated by cesarean section. One of the cases was a central placenta previa and was treated by insertion of Voorhees' bag and subsequent version and extraction. The blood loss during both of these procedures was 1,200 c.c.

TABLE II. SHOWING RELATION OF BLOOD LOSS TO AGE OF PATIENT

AGE		HEMORRHAGES		AVERAGE
	CASES	CASES	PER CENT	BLOOD LOSS
Less than 20 years	33	0	0.00	183 c.c.
20-29 years	337	21	6.23	220 с.с.
30-34 years	79	6	7.60	266 с.с.
Over 34 years	51	5	9.80	279 с.с.

Of particular interest were the fifteen patients whose hemoglobin prior to delivery was less than 70 per cent. Four of these patients had blood losses of 600 c.c. or more, and the average blood loss was 456 c.c. This brings out the necessity of following closely the hemoglobin during the antepartum course. One determination at the time of registration is not enough, and at least one more reading should be obtained during the last month of pregnancy. Other obstetric and systemic complications showed no appreciable increase in blood loss.

Parity and Gravidity.—Table III discloses a marked increase in the blood loss in patients who have had two or more abortions. The incidence of hemorrhage in this group was 13.78 per cent with an average loss of 318 c.c. Parity seems to have very little effect, except in the primiparas, as the incidence of hemorrhage would be reduced to 4.34 per cent if the thirty-eight patients who had had previous abortions are excluded from the group.

Table III. Showing Relation of Blood Loss to Parity and Previous Abortions

	CASES	HEMORRHAGES		AVERAGE	
		CASES	PER CENT	BLOOD LOSS	
Primipara	269	15	5.57	261 c.c.	
Multipara	231	17	7.35	248 c.c.	
Para i	128	11	8.59	264 c.c.	
Para ii or more	103	6	5.82	228 c.c.	
No previous abortions	404	24	5.94	251 c.c.	
1 previous abortion	67	4	5.95	251 c.c.	
2 or more abortions	29	4	13.78	318 e.c.	

Toxemia of Pregnancy.—There were fifty-four cases of toxemia in this series, with three hemorrhages or an incidence of 5.55 per cent. The low reserve kidney group alone showed a slight increase to 8.59 per cent with an average loss of 253 c.c. The six cases of chronic nephritis showed an unusually low average loss of 150 c.c. The other forms of toxemia showed no effect on the blood loss.

Duration of Labor.—Although the total duration of labor has some slight effect on the blood loss, the more marked effects are obtained with prolongation of the second and third stage, as shown in Table IV. There is almost 40 per cent increase with second stage labor of over ninety minutes. Over 50 per cent increase is noted in third stage of over thirty minutes. No attempt was made in our series to study the effect of the intensity and frequency of the contractions as has been done recently by Calkins. However, it was noted that in thirty cases of contracted pelvis there were no hemorrhages and the average loss was 260 c.c. The various vertex presentations showed no appreciable difference in blood loss. The breeches, however,

showed an increase to 17.64 per cent, with an average loss of 291 c.c. It can be concluded, therefore, that whatever factors, other than contraction of the pelvis, are responsible for the prolongation of the second and third stage of labor are also responsible for the increased blood loss.

TABLE IV. SHOWING RELATION OF BLOOD LOSS TO THE DURATION OF LABOR

	a and	HEMO	RRHAGES	AVERAGE
	CASES	CASES	PER CENT	BLOOD LOSS
Total Duration:				
3 hours or less	28	1	3.57	214 с.с.
3 to 10 hours	211	15	7.10	240 c.c.
10 to 30 hours	224	12	5.35	268 c.c.
Over 30 hours	37	4	10.81	269 c.c.
Second Stage:				
11 hr. or less	404	23	5.69	239 с.с.
Over $1\frac{1}{2}$ hr.	96	9	9.37	325 c.c.
Third Stage:				
Under 3 minutes	26	1	3.80	246 e.e.
3 to 30 minutes	440	24	5.45	245 c.c.
31 to 60 minutes	28	5	17.86	364 c.c.
Over 60 minutes	6	2	33.33	483 c.c.

Induction of Labor.—No direct effect was found in forty-five patients who had received medical induction. The average loss was 285 c.c. and the incidence of hemorrhage 4.44 per cent. Only one patient in this series had an operative induction so that no conclusions can be drawn.

Analgesia During Labor.—Considerable emphasis has been placed on analgesia and anesthesia as the cause of excessive blood loss during the third stage of labor. Recently Calkins has changed Kerr and Ferguson's statement to read, "We are absolutely satisfied that the two important causes of postpartum hemorrhage are faulty management of the third stage and large doses of anesthetic and sedative drugs." For this reason an analysis of the various medications was made and the results are presented in Table V. In dividing the cases into two groups, those with and those without analgesia, we find very little difference in the average blood loss or the incidence of hemorrhage. However, there are marked variations with the various forms of analgesia. It is significant, I think, that the highest incidence of hemorrhage and average blood loss was obtained in that group of patients who had received morphine and rectal ether. In fifty-six cases in this group hemorrhages were noted in 12.5 per cent of the patients and the average loss was 332 c.c. Even in those cases where rectal ether alone was administered the loss is greater than

TABLE V. SHOWING THE EFFECT OF ANALGESIA ON THE BLOOD LOSS

	0.000	HEMORRHAGES		AVERAGE	
	CASES	CASES	PER CENT	BLOOD LOSS	
Without analgesia	272	19	6.98	241 c.c.	
With analgesia	228	13	5.70	272 c.c.	
Morphine alone	31	1	3,22	261 c.c.	
Morphine and scopolamine	22	0	0.00	213 c.c.	
Rectal ether alone	69	4	5.79	271 c.c.	
Morphine and rectal ether Morphine, scopolamine and	56	7	12.50	332 c.c.	
rectal ether	41	1	2.44	247 c.c.	
Nembutal alone	1	. 0	0.00	50 c.c.	
Nembutal and others	8	0	0.00	225 c.c.	

with other forms of therapy. However, when scopolamine is given prior to the administration of rectal ether the blood loss is markedly reduced. What rôle the scopolamine plays in the contraction of the uterus I am unable to state at this time, but that it does reduce the blood loss seems quite evident from this study. Recently, C. R. Tew, in a study of 400 cases of rectal ether analgesia in this clinic, reported no significant increase in the incidence of hemorrhage. This discrepancy can be explained on the basis of estimation of the blood loss, or to the routine use of scopolamine. At the time his study was conducted the blood loss was not measured. A series with paraldehyde analgesia is now being tried.

Anesthesia.—Table VI shows the effects of the various forms of anesthesia used during the second and third stages. Here again ether increases the blood loss. Ether anesthesia may also account for part of the loss occurring during repair of episiotomies and lacerations.

TABLE VI. SHOWING EFFECTS OF ANESTHESIA ON BLOOD LOSS

ANESTHESIA	CASES	HEMORRHAGES		AVERAGE
		CASES	PER CENT	BLOOD LOSS
None	4	0	0.00	125 c.c.
Nitrous oxide alone	308	14	4.54	232 с.с.
Nitrous oxide and ether	185	17	9.18	292 c.c.
Ether alone	3	1	33.33	483 c.c.

Rupture of the Membranes.—Ahlfeld and others repeatedly have stated that the time of rupture had no influence on the blood loss. In Table VII a study of the time of rupture in the 500 cases shows a direct effect on the blood loss. Premature rupture of the membranes increases the incidence of hemorrhage by over 50 per cent and the average loss by 30 per cent. In fact, it can be said that the later the rupture the less the bleeding. The cases with rupture during the first and second stages include both the spontaneous and the artificial ruptures.

TABLE VII. SHOWING RELATION OF BLOOD LOSS TO THE RUPTURE OF THE MEMBRANES

RUPTURE OF THE		HEMO	AVERAGE	
MEMBRANES	CASES	CASES	PER CENT	BLOOD LOSS
Second stage	234	11	4.70	236 с.с.
First stage	145	10	6.89	261 c.c.
Prematurely	90	9	10.00	299 c.c.
Unknown	31	2	6.43	243 c.c.

This study also offered the opportunity to evaluate the often quoted statement that premature rupture of the membranes increases the incidence of puerperal infection. In the 90 cases of premature rupture of the membranes there was an incidence of 14.44 per cent of febrile puerperium in contrast to 13.17 per cent in the 410 cases without premature rupture. This increase is within the expected limits, since we had a 50 per cent increase in hemorrhage and we know from Fig. 3 that 34.37 per cent of the hemorrhage group have a febrile puerperium. In addition the incidence of morbidity in the cases without hemorrhage is practically the same for both groups: 12.34 per cent with premature rupture, and 11.88 per cent without premature rupture. Also, the incidence of morbidity in the nine cases of hemorrhage with premature rupture was 44.44 per cent in contrast to 30.43 per cent in those without premature rupture. This too is a 50 per cent increase. It can be said: that premature rupture of the membranes definitely increases the blood loss by about 50 per cent; that with no excessive blood loss the incidence of infection is not

increased; and that with hemorrhage the incidence of morbidity is also increased by about 50 per cent. Can we assume then, that morbidity is directly proportional to the lowered resistance obtained with excessive blood loss?

Type of Delivery.—As shown in Table VIII, operative delivery is accompanied by increased blood loss during the third stage. The incidence of forceps delivery in the series was 10.2 per cent with an average loss of 405 c.c. and an incidence of hemorrhage of 11.76 per cent. The incidence of breech delivery was 3.4 per cent

TABLE VIII. SHOWING RELATION OF BLOOD LOSS TO TYPE OF DELIVERY

TYPE OF DELIVERY		HEMORRHAGES		AVERAGE	
	CASES	CASES	PER CENT	BLOOD LOSS	
Full term	488	32	6.55	257 c.c.	
Premature	12	0	0.00	175 e.e.	
Spontaneous	430	21	4.89	234 c.c.	
Operative	70	11	15.71	385 c.c.	

with an average loss of 291 c.c., and an incidence of hemorrhage of 17.64 per cent in the seventeen cases. The operative cases accounted for one-third of the hemorrhages. The indications for the operative procedures were studied and no definite effect could be found. There were only four midforceps and one high forceps in the series.

Presentation of the Placenta.—Schultze presentation of the placenta was encountered in 70.22 per cent of the cases with an average loss of 231 c.c. and an incidence of hemorrhage of 4.67 per cent. In 29.68 per cent of the cases the placenta presented by the Duncan mechanism with an average loss of 269 c.c. and 5.51 per cent hemorrhages. This does not include the thirteen cases in which manual removal of the placenta was carried out and in which the presentation of the placenta could not be differentiated.

The morbidity with manual removal of the placenta is presented in Table IX. The five patients without hemorrhage had an average loss of 390 c.c., and the

TABLE IX. SHOWING THE PUERPERIUM IN MANUAL REMOVAL OF THE PLACENTA

POSTPARTUM COURSE	1	THOUT ORRHAGE	WITH HEMORRHAGE	
	CASES	PER CENT	CASES	PER CENT
Afebrile	4	80.0	4	50.0
Febrile	1	20.0	3	37.5
One day fever	0	0.0	1	12.5

incidence of morbidity was no greater than in cases of spontaneous delivery of the placenta with the same blood loss. The incidence in the hemorrhage group is also within the expected limits. Our impression that manual removal of the placenta leads to puerperal infection is probably based on the fact that in the past it was resorted to only as a last procedure and the patient was already in critical condition. The series is too small to draw definite conclusions, but if these results are substantiated in future studies, it would justify the manual removal of the placenta in cases where postpartum hemorrhage seems inevitable.

Subinvolution of the Uterus.—Subinvolution occurred in 15.62 per cent of the cases with hemorrhage in contrast to 13.24 per cent of the cases without hemorrhage. The incidence is even higher in the hemorrhage group because these patients remained in the hospital longer and consequently their discharge examination was done later.

Weight and Length of Baby.—The relation of blood loss to the weight of the baby is shown in Table X. There is a progressive increase in the blood loss and incidence of hemorrhage with increase in weight, as was first shown by Ahlfeld. This has been ascribed to the overdistention of the uterus, but Ahlfeld suggested

TABLE X. SHOWING RELATION OF BLOOD LOSS TO THE WEIGHT OF THE BABY

	a.como	HEMORRHAGES		AVERAGE
WEIGHT OF BABY	CASES	CASES	PER CENT	BLOOD LOSS
Less than 2500 gm.	28	0	0.00	164 c.c.
2500-2999 gm.	88	3	3.40	198 c.c.
3000-3499 gm.	167	. 7	4.19	234 с.с.
3500-3999 gm.	156	15	9.61	285 c.c.
4000 gm, and over	61	7	11.47	359 с.с.

that in reality it was due to the large placentas associated with large babies. Our study of the weight and size of the placenta, however, did not bear this out.

The same tabulation was made for the length of the baby but this showed no correlation with the blood loss.

Lacerations of the Perineum and Cervix.—The study of the blood loss with lacerations, as revealed in Table XI, shows a marked increase with the extent of the laceration. In our series episiotomies bled about 100 c.c. more than the average for the 500 cases, or 150 c.c. more than those without lacerations. Recently Calkins stated that the average increase in blood loss with episiotomies was only about 60 c.c. and that it seldom offered a severe complication. To those of us who have used our present apparatus for measuring the blood loss, it has been obvious that there is considerably more bleeding with episiotomies and lacerations than we had formerly thought. With Calkins' method it is impossible to collect the blood during the repair and this undoubtedly accounts for some of the discrepancy. The anesthesia used during the repair contributes to some of the blood loss, and we have had several cases of hemorrhage in which the major part of the loss was due to the episiotomy.

TABLE XI. SHOWING THE EFFECTS OF LACERATIONS ON THE BLOOD LOSS

T A CERT A MY CATCO	CASES	HEMORRHAGES		AVERAGE	
LACERATIONS		CASES	PER CENT	BLOOD LOSS	
None	208	10	4.80	200 c.c.	
First degree	107	3	2.80	231 c.c.	
Second degree	53	3	5.66	316 c.c.	
Episiotomy	131	16	12.21	351 c.c.	
Third degree	1	0	0.00	450 c.c.	
Cervical	3	2	66.66	783 c.c.	

For that reason lacerations and episiotomies should be repaired immediately in those cases where there is active bleeding. The anesthesia of course will effect the third stage, and it would seem that in these cases pituitrin given before the delivery of the placenta would be justified, although this has not been our practice.

Weight of the Patient.—As shown in Table XII the weight of the patient has marked influence on the blood loss. There is some discrepancy in the first group, but this only includes 4 patients. The weight of the patient, as the hemoglobin prior to delivery, has great prognostic value. Obviously a patient of 90 kilograms will react far better to a loss of 1,000 c.e. than will one of 50 kilograms. This factor is too often neglected in the postpartum treatment of the patient.

Weight and Diameter of the Placenta.—Tabulation of the blood loss in relation to the weight and the mean diameter of the placenta showed no definite correlation, contrary to the findings of many observers. Apparently there was no relation be-

tween the weight of the placenta and the weight of the baby as the results should have agreed with those in Table X.

Twin Pregnancy.—In this series there was only one case of multiple pregnancy with a blood loss in the 500 c.c. group. No conclusions can be drawn from this, but earlier investigators have shown an increased blood loss.

TABLE XII. SHOWING RELATION OF BLOOD LOSS TO THE WEIGHT OF THE MOTHER

	CASES	HEMORRHAGES		AVERAGE	
WEIGHT OF PATIENT		CASES	PER CENT	BLOOD LOSS	
41 to 50 kg.	4	1	25.00	350 с.с.	
51 to 60 kg.	85	1	1.17	183 c.c.	
61 to 70 kg.	205	7	3.41	225 c.c.	
71 to 80 kg.	130	13	10.00	311 с.с.	
81 to 90 kg.	46	6	13.04	330 c.c.	
91 to 100 kg.	13	2	15.38	335 c.c.	
Over 100 kg.	12	2	16.66	315 e.c.	
Unknown	5	0	0.00	150 c.c.	

THE POSTPARTUM HEMORRHAGE GROUP

The various causes for the 32 cases of hemorrhage are indicated in Table XIII.

TABLE XIII. CAUSES OF POSTPARTUM HEMORRHAGE

CASES	PER CEN'
12	37.500
8	25.000
3	9.375
3	9.375
2	6.250
2	6.250
1	3.125
1	3.125
20	100,000
	12 8 3

In seven of the eight cases of incomplete separation of the placenta, manual removal was resorted to and the diagnosis confirmed. Most of the bleeding in these cases occurred before the removal of the placenta. It is interesting to note that in five of these cases the patients received nitrous oxide and ether for the repair of the episiotomies. In addition two of the five had breech extractions which also necessitated the use of ether. It seems plausible that ether should interfere with the normal contraction of the uterus and therefore may be responsible for the partial separation of the placenta. Obviously some of the placenta must be separated during the delivery of the baby as the uterus contracts to at least one-half its normal size at term. The degree of separation depends on the degree of contraction of the uterus which in turn is influenced by anesthesia. The average duration of the third stage in these eight cases was twenty-seven minutes. The same situation is present in those cases where just prior to delivery the fetal heart becomes irregular due to strong contractions of the uterus. The usual procedure is to administer ether anesthesia and to deliver the patient as soon as possible. Invariably the third stage in these cases is associated with a high incidence of incomplete separation of the placenta and excessive blood loss.

The three cases of uterine atony also had ether and nitrous oxide during the repair of episiotomies in two of them, and during the repair of a first degree laceration with ruptured varicosities in the third case. In the group described as mismanagement are included all cases in which the major portion of the bleeding occurred with the expression of the placenta. This cause occurred more frequently during the early part of this study as most of the men were not familiar with Calkins' technic for determining the separation of the placenta. It is due to lack of recognition of the separation of the placenta and can be reduced by proper training.

Two of the hemorrhages were due to prolapse of the fundus deep into the pelvis. This type of bleeding can also be reduced by proper management of the third stage and will be discussed later in this paper.

Further study of the puerperium in the cases with excessive blood loss revealed that of the eleven patients with febrile course only three had hemoglobin determinations postpartum of 70 per cent or over. The highest determination was 72 per cent, and there were five patients with less than 60 per cent. In contrast to this only seven out of the sixteen patients with afebrile courses had hemoglobin determinations of less than 70 per cent. In the one day fever group of five cases three were below 70 per cent. There is a definite relationship between morbidity and the drop in hemoglobin after delivery. The drop in hemoglobin is dependent upon the blood loss and the weight of the patient. This exact coefficient cannot be determined from this study, but experiments are now being conducted to determine this factor. It will be of great value at the time of delivery to be able to compute the drop in hemoglobin and thus select the patients who should have transfusions.

THE MANAGEMENT OF THE THIRD STAGE

The proper management of the third stage is directly proportional to the individual's training and experience. The greater portion of hemorrhages in our service usually occurs during the first two weeks of service of each new interne. The junior internes have a greater incidence than the senior members in normal spontaneous deliveries.

Most observers are agreed that the views formerly held by Ahlfeld, Polak, and others are not tenable, and that the placenta should be expressed immediately after its separation as first advocated by Williams. The main difficulty, however, lies in the correct diagnosis of the separation of the placenta. The classical signs as given in the textbooks are present only after some time has elapsed after the separation.

Calkins in 1933, by a modification of the Williams technic, was able to reduce his average blood loss from 210 c.c. to 179 c.c. We have found this method of great value during this study, and it has proved that the duration of the third stage is much shorter than was formerly believed. This method, as stated in C. H. Davis' Gynecology and Obstetrics, places great emphasis on the change of shape of the uterus following delivery of the child. Immediately following the delivery of the baby, the uterus assumes a discoid or flattened shape. When the placenta is separated it assumes a globular shape and the placenta is expressed with the next contraction.

Of even greater importance in reducing the blood loss is the method of expression of the placenta. It has been shown repeatedly that there is increased bleeding following delivery of the placenta if the fundus is pushed deep into the pelvis. This is primarily due to partial obstruction of the venous drainage of the uterus as so often occurs in

retroversion of the uterus in the nonpregnant state. Most writers call attention to its significance following delivery of the placenta, but very little has been done toward its prevention. With the use of the Brandt maneuver its occurrence is greatly reduced, but it does not seem wise to attempt this maneuver without the diagnosis of separation of the placenta, as is recommended by the author. In addition it offers no protection against partial inversion of the uterus over the top and the posterior surface of the uterus. For that reason we have modified Calkins' technic as follows: Immediately following the delivery of the child, the right hand of the assistant is placed over the top of the fundus with the thumb over the anterior and the fingers over the posterior surface of the uterus. When the placenta is separated the fundus is gently massaged or, if there is no bleeding present. it is left alone until a contraction occurs spontaneously. At this time the left hand of the assistant is placed flat over the abdomen with the fingers directed under the symphysis. The fundus is then squeezed and pushed downward with the right hand. The left hand prevents the fundus from entering the pelvis. The placenta can be felt passing through the cervix and at this time the fundus is held up while the operator extracts the placenta from the vagina. There is no necessity for pushing the placenta out of the vagina at the expense of uterine trauma. If the placenta is not completely out of the cervix, the cord is held by the operator while the fundus is lifted up by the assistant. By the use of this method we have reduced the bleeding due to prolapse of the fundus into the vagina. The placenta should be expressed immediately after its separation and not after the conclusion of the repair of perineal lacerations or episiotomies.

Continued bleeding from the uterus prior to the delivery of the placenta is indicative of partial separation. This condition is brought about primarily by the use of anesthesia at the time of delivery and during repair of lacerations, or by the unwarranted attempts at expression of the placenta. Regardless of the cause, in the face of rapidly increasing blood loss as shown' by the manometer, manual removal should be seriously considered. Manual removal of the placenta under ideal conditions offers the same prognosis as the blood loss associated with it.

Following delivery of the placenta continued bleeding from the vagina is due to four possible causes and each can be eliminated quickly, as follows:

1. Uterine atony, due either to lack of contraction or the presence of fibroids or retained placenta, particularly succenturiate lobes. The assistant is able to eliminate this cause instantly and the various forms of stimulations should be used. Intravenous pituitrin, 1½ minims in 5 c.e. of saline, can be given safely if it is given slowly, and has never failed in this series to cause immediate contraction.

- 2. Prolapse of the fundus into the vagina. This should be eliminated by the proper management of the expression of the placenta. In all cases the fundus should be held out of the pelvis and such bleeding stops immediately. Occasionally, if the cervix is practically out of the vagina, it may be necessary for the operator to apply pressure on the cervix in order to raise it out of the pelvis.
- 3. Perineal lacerations. By inspection the source of the bleeding can be determined and proper measures instituted. Ruptured varicosities are better treated by packing than attempts at repair. Muscle sutures should be placed first in bleeding lacerations or episiotomies.
- 4. Cervical lacerations. This, of course, can be controlled only by proper sutures. However, I do not believe in the routine inspection of the cervix unless the above three causes have been ruled out. Only too often the bleeding is due to prolapse and this is accentuated by inspection of the cervix.

For teaching students this offers a rapid method for the proper diagnosis. In persistent atony of the uterus, packing should be resorted to. It was carried out in two cases in this series, one for placenta previa, and the other for myoma of the uterus. With the use of the Holmes' packer infection is reduced to a minimum. The packing can be removed slowly in most cases within six to twelve hours, although there is no particular danger in leaving the packing in for twenty-four hours.

The usual treatment for shock should be employed when indicated. It should be remembered, however, that intravenous fluids, if used before the cause of the bleeding has been corrected, will cause additional bleeding and more profound and serious shock. Transfusions should be given immediately in cases of excessive blood loss. The usual tendency is to "wait and see what the hemoglobin does." However, at that time the patient usually has a fever and one hesitates to give a transfusion. Until we can predict the drop in hemoglobin postpartum, it will be difficult to say which case should have a transfusion. Supportive measures offer no immediate effects to maintain the patient's resistance against infection.

SUMMARY

A study of the third stage of labor in 574 consecutive vaginal deliveries is presented. Seventy-four cases were excluded because the blood loss was not completely measured. In the 500 cases studied, the blood loss was measured by the method recently described by the author. The various factors responsible for excessive blood loss have been presented. A study of the puerperium has also been made. Comparison of estimated and measured blood losses revealed that estimations are erroneous and misleading. The author's method of expression of the placenta is also presented. Further study of at least 2,000 more cases is necessary to substantiate the conclusions drawn from this study.

CONCLUSIONS

- 1. The incidence of postpartum hemorrhage was 6.4 per cent with an average blood loss of 244.3 c.c. There were 70.4 per cent of the patients who had a loss of less than 300 c.c.
- 2. The incidence of puerperal infection rises with increase in blood loss. The duration of stay in the hospital follows a similar curve.
- 3. Anemia predisposes to excessive blood loss. Patient's hemoglobin prior to delivery and the patient's weight have great prognostic value in the treatment of hemorrhage.
 - 4. Previous abortions influence the blood loss during the third stage.
- 5. Premature rupture of the membranes increases the bleeding by about 50 per cent. The increase in morbidity with premature rupture of the membranes corresponds with the increase in blood loss.
- 6. Manual removal of the placenta predisposes to no more morbidity than is present with the associated blood loss.
- 7. Mismanagement of the third stage, partial separation of the placenta, and uterine atony were responsible for over 71 per cent of the hemorrhages. Anesthesia is partly responsible for the partial separation and the uterine atony.
- 8. The experience and ability of the operator and his assistants have a marked effect on the blood loss. The correct diagnosis of the separation of the placenta and the proper expression of the placenta will reduce the number of hemorrhages due to mismanagement of the third stage.

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THE TREATMENT OF PELVIC INFLAMMATION BY IONTOPHORESIS OF ACETYL-BETA-METHYLCHOLINE-CHLORIDE

ADOLPH JACOBY, M.D., F.A.C.S., NEW YORK, N. Y.

(From the Department of Gynecology, New York Post-Graduate Medical School and Hospital, Columbia University)

THE most important principle in the nonoperative treatment of pelvic inflammation is the induction of pelvic hyperemia. It is most easily accomplished by hot douches, taken properly. A modification of this therapeutic agent is applied in the Elliott treatment, in which the hot water is enclosed in a rubber bag in the vagina. The Elliott vaginal hot water bottle makes it possible to use higher degrees of temperature. Various external heating devices, such as electric light hoods, heat cabinets, and heat lamps have also been employed to initiate hyperemia. Diathermy has become a popular method of treatment, and is utilized to project heat between two electrodes, one in the vagina and the other on the abdomen. The radiotherm, or high-frequency fever producing machine, excites a general elevation of temperature and, with special technic, an incidental localized hyperemia.

Recently a group of drugs has been made available, each of which produces vasodilatation and thus induces hyperemia. Among such drugs are acetylcholine, histamine, and acetyl-beta-methylcholine-chloride.*1 Of these acetyl-beta-methylcholine-chloride, the latest compound produced, seems to be the most effective.

Acetyl-beta-methylcholine-chloride when taken by mouth in doses of 100 to 200 mg., produces generalized flushing and sweating, increased salivation, a lowering of blood pressure, increase in pulse rate, intestinal peristalsis, and metabolism, which last from one-half to one hour.² Subcutaneously in doses of from 5 to 25 mg. the same effects are greatly increased and last from fifteen to twenty minutes except that the action on the gastrointestinal tract is not so pronounced.³

When applied locally by iontophoresis,⁴ there is some general reaction, but a much more pronounced effect at the site of application. This is particularly true in doses of 0.2 to 0.3 gm. When applied to the skin, the drug causes a rise in skin temperature for two to eight hours, marked sweating for four to ten hours, slight redness, a faster rate of capillary flow, and a slight increase in the white blood cell count. The marked vasodilatation is due chiefly to its effect on the arterioles.⁵

^{*}The Acetyl-Beta-Methylcholine-Chloride (Mecholyl) was supplied by Merck & Co. Inc.

Table I. Effect and Dosage of Vasodilating Drugs by Different Methods of Administration

DRUGS	ACETYL-BETA-METHYLCHOLINE	ACETYL CHOLINE	
Oral	Mild general effect, lasts ½ to 1 hour. Dose, 100 to 200 mg.	None	
Subcutaneous	Powerful general effect, lasts 15 to 20 minutes. Dose, 5 to 25 mg.	Mild general effect, lasts 15 to 20 minutes. Dose, 100 to 200 mg.	
Intravenous	Dangerous, toxic		
Iontophoresis	Pronounced general effect lasts 20 to 40 min. Pronounced local effect lasts 4 to 10 hours. Dose, 0.5 to 1 per cent solution	Mild general effect, lasts 10 to 20 minutes Mild local effect, lasts 1 to 2 hours. Dose, 0.5 to 1 per cent solution	

Table II. Comparative Physiologic Effects of Mecholyl and Histamine Iontophoresis

	MECHOLYL ACTION MOSTLY ON ARTERIOLES	HISTAMINE ACTION MOSTLY ON CAPILLARIES	
Topical effects	Increased skin temperature for 2 to 8 hours, Increased sweating for 4 to 10 hours. "Goose-flesh" lasting 10 to 20 minutes. Increased oscillometric reading. Fast- er capillary flow. Slight redness. Slight increase in local white blood cell count	Increased skin temperature for 2 to 4 hours. Enlarged capillaries. Increased cap illary permeability. Wheal formation. Faster capil- lary flow. Definite redness	
Systemic effects	Flush, sweating, increased salivation, lowered blood pressure, increased pulse rate, increased intestinal peristalsis, increased metabolism. Electrocardiogram: PR conduction time increased, Twave increased amplitude, rate slower. Effects last 20 to 40 minutes	None	

These physiologic effects have been utilized with considerable success in the treatment of spastic vascular conditions, endarteritis obliterans and infectious arthritis. The good results in such cases suggested the likelihood of effecting the same physiologic reactions to advantage in the pelvis, provided they could be induced by vaginal applications of the drug. To determine the possibilities involved in this theory, the treatment of various types of pelvic inflammation with acetyl-beta-methyl-choline-chloride was attempted by introducing the drug through the vaginal vault by iontophoresis.

TECHNIC

With the patient in the lithotomy position, a bivalve speculum is inserted and the vaginal vault exposed. All excess of secretion is wiped away. Several thicknesses of gauze 6 inches square are soaked in 20 c.c. of a 1 per cent solution of acetyl-beta-methylcholine-chloride, prepared by dissolving 1 gm. of drug in 100 c.c.

of distilled water. This square of impregnated gauze is carefully spread out against the entire vault of the vagina. A thin vaginal electrode, with the active end wrapped in gauze and soaked in the 1 per cent choline solution is placed firmly against the gauze pack. The speculum is withdrawn leaving the electrode in place. This electrode is attached to the positive pole of a galvanic apparatus. A flat dispersive pad 6 by 8 inches, well moistened in warm water, is placed on the lower abdomen and connected to the negative pole. To insure an even contact, a sand-

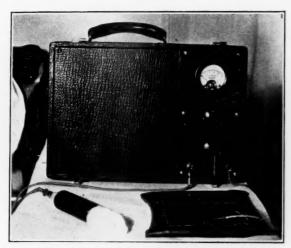


Fig. 1.—Galvanic machine. Vaginal electrode wrapped with gauze. Flat abdominal electrode,

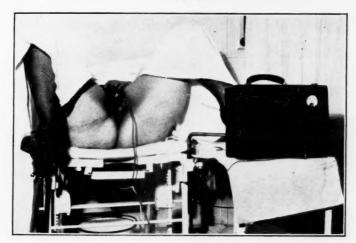


Fig. 2.—Technic of application. Vaginal electrode to the positive pole and abdominal electrode to the negative pole.

bag is placed over the negative pad and the patient is directed to press it firmly against the skin. The current is turned on gradually until 15 or 20 milliamperes are used, and allowed to flow for twenty to thirty minutes. The current is then slowly shut off and the electrode and vaginal gauze removed. The amount of acetylbeta-methylcholine-chloride thus introduced has been found to be 31 per cent, or 62 mg. Allowing for the small quantity which adheres to the vaginal wall, this corresponds closely with the estimated amount of 24 per cent or 48 mg., which should

theoretically be introduced by this technic. No douches are prescribed at any time. The treatment is repeated every other day. No local reaction is noticed by the patient, but there is usually a generalized sweating, flushing, and sense of warmth, with marked salivation during the treatment. In some instances there is an initial drop of blood pressure. When the general reaction is too pronounced, the application is interrupted, and 1/150 gr. atropine sulphate is given hypodermically. This acts as a physiologic antidote and immediately counteracts all untoward symptoms.

A brief transcript of the results obtained in the first ten patients treated is appended herewith.

Case 1.—(A61574) P. C., married nine years, 2 children, youngest three years old, no miscarriages, menstruation regular, six or seven days, moderate amount accompanied by pain. Complained of pain in left upper and lower abdominal quadrants, four to five months' painful menstruation. Vagina relaxed. Cervix lacerated. Uterus normal. Right adnexa negative. Left tube and ovary enlarged and tender. Parametrium posteriorly thickened. Cervicitis, left salpingo-oophoritis, posterior parametritis. She had eleven treatments from Dec. 5, 1933 to Jan. 6, 1934. On Jan. 19, 1934, cervix smooth. Uterus negative. Adnexa negative. Parametrium soft, not sensitive. Menstruation painless. On June 14, 1934, pelvic examination was negative. Still complained of upper abdominal pain. Referred to Gastro-Intestinal Department.

Comment: This patient had a subacute pelvic inflammation. Treatment afforded complete relief of pain during menstruation and disappearance of the inflammatory exudate after thirty-two days. Upper abdominal symptoms persisted.

CASE 2.—(A58588) M.F., thirty-three years old, married fourteen years, no children, no miscarriages, menstruation regular, three to four days, moderate amount, painful. Pain in lower abdomen for fourteen years, more severe during menses. Moderate discharge. June 22, 1933, vagina negative. Cervix slight erosion. Slight discharge. Few cysts. Aug. 26, 1933, endocervix removed by conization. Three weeks later the right tube and ovary was enlarged and adherent, extending to pelvic wall and posterior surface of uterus. Chilliness and fever. Dec. 9, 1933, the mass continued its extension behind the uterus and to the left border of the pelvis. Parametrium thick and tender.

Diagnosis: Bilateral salpingo-oophoritis, parametritis. She received 7 treatments starting Dec. 12, 1933, and ending Jan. 6, 1934.

On Jan. 6, 1934, right adnexa negative. Ovary palpable. Left tube negative. Left ovary slightly enlarged. Exudate entirely disappeared. The same findings were present on reexamination March 3, 1934, and June 16, 1934.

Comment: This patient had an adnexal inflammatory flare-up following cervical conization. Completely cured in twenty-five days.

Case 3.—(80477) A. N., thirty-five years of age, married seventeen years, 2 children, youngest two years old, no miscarriages, menstruation regular, four days, moderate, no pain. Discharge yellow and white, one year. July 19, 1933, vagina relaxed. Cervix reddened and lacerated. Uterus anterior. Adnexa negative. Endocervicitis. Nov. 16, 1933, endocervix removed by conization, and later several nabothian cysts were destroyed by cautery. She developed increasing pain in left lower abdominal quadrant during the past ten weeks. Feb. 24, 1934, uterus anterior, close behind symphysis, normal size, pushed to the right. To the left of the uterus is a large mass filling the entire pelvis rising above the uterine fundus, extending backward behind the uterus and toward the right. Feels cystic, fixed, and tender. Diagnosis: Probable tuboovarian inflammation (possible ovarian cyst). She received 9 treatments from Feb. 27, 1934, to March 22, 1934. After two treatments mass

one-fourth its original size. On March 24, 1934, uterus freely movable, normal size and position. Right tube and ovary negative. Left tube negative. Left ovary palpable, prolapsed, not sensitive, freely movable. Reexamination on May 19, 1934, was entirely negative.

Comment: This patient had an adnexal flare-up following cervical conization and cauterization of cysts. Exudate disappeared entirely in twenty-three days.

Case 4.—(A77218) H. M., thirty-seven years of age, married twelve years, widow five years, one child sixteen years old, no miscarriages, menses regular, four days, painful. Moderate yellow discharge for five years. Pain in the back and right lower quadrant for sixteen years. Vagina relaxed. Cervix lacerated, moderate purulent discharge. Uterus negative. Adnexa negative. Diagnosis: Cervicitis. On March 1, 1934, cervix was coagulated. Three weeks later she had severe pain in lower abdomen, chills, and fever. Cervix: slight slough in external os. Uterus slightly enlarged. Adnexa on both sides enlarged, extending to the pelvic walls and adherent. Parametrium densely infiltrated. Diagnosis: Bilateral salpingooophoritis, pelvic cellulitis. Temperature 102.2° F. by mouth. Pulse 104. Blood count 3,830,000 red blood corpuscles. Hemoglobin 84 per cent. White blood corpuscles 38,000. Polynuclear leucocytes 89 per cent. March 27, 1934, admitted to hospital. Ran an elevated temperature for six days, highest 104° F. On seventh day temperature was 99.6° F. and normal thereafter. In the hospital for fifteen days. She had 5 treatments. In addition, had ice bag to the lower abdomen, on two hours and off two hours, and hot saline douches. She was discharged from hospital on April 7. Examination on that day showed cervix smooth, and uterus anterior, tilted to the left. Left tube and ovary negative. Right tube very slightly thickened. No adhesions. No tenderness. Parametrium free of all exudate.

Comment: This patient had an acute pelvic inflammatory reaction following coagulation of cervix. Exudate disappeared entirely after treatment for fifteen days.

CASE 5.—(A77724) C. T., twenty-two years of age, married, no children; menses regular, two days, moderate, no pain. Pain in left lower quadrant, 5 days, moderate yellow discharge two weeks, backache. External genitals irritated. Vagina irritated. Cervix small. Uterus close under the symphysis. Right tube and ovary slightly thickened and sensitive. Left tube and ovary markedly enlarged, filled the entire left pelvis, about four inches in diameter, extended behind the uterus, irregular in outline, somewhat soft, immobile, and tender. Parametrium thickened and sensitive posteriorly. Bilateral salpingo-oophoritis. Probable left pyosalpinx. She received 8 treatments from Feb. 3 to March 6, 1934. After three treatments mass on left side one-third original size. Fornices free. No fluctuation. Adnexal structures becoming isolated. On March 6, 1934, slight thickening in right fornix. Pelvis otherwise negative. On March 15 uterus small, normal position, freely movable. Adnexa negative. No exudate or thickening in the pelvis.

Comment: This patient had an acute bilateral pelvic adnexal inflammation, probably of specific origin, with pus in the left tube. The exudate entirely disappeared after treatment for thirty-one days.

Case 6.—(A71352) F. S., twenty-three years of age, married six years, one child three years ago, died at birth; two miscarriages, menstruation one day, slight amount, painful. Profuse mucopurulent discharge. Sharp pain in right lower quadrant for two weeks. Frequent urination day and night. Cervix reddened, profuse discharge. Uterus anterior. Adnexal mass filling right fornix, tender, thickened about three inches in diameter. Left tube thickened and tender. Parametrium thickened. Cervicitis, bilateral salpingo-oophoritis, parametritis. She had 6 treatments from Jan. 18 to Feb. 15, 1934. Feb. 1, 1934, had two treatments.

Menstruated on January 22 for two days, stopped for two days, started again January 27 to 31. Had severe backache. Examination showed adnexal masses diminishing in size. Cervical discharge diminished. Treatment resumed. On February 15, tubes not palpated on either side. Apparently normal. Right ovary slightly enlarged. Left ovary normal. Uterus freely movable, no pain, no tenderness. Patient apparently well. On February 24, menstruated for two days. Some pain in lower abdomen. Examination entirely negative. On March 10, menstruated four days, no pain. Examination negative. Reexamination, June 5, negative.

Comment: This patient had a subacute bilateral pelvic inflammation, probably specific. The exudate cleared up entirely after twenty-eight days' treatment.

Case 7.—(A82503) F. C., forty-one years of age, married twenty-four years, one child twenty years old, 5 miscarriages, last one twenty-one years ago, menstruation irregular and profuse. Pain in left lower quadrant six years ago. Pain in both lower quadrants for two months. Backache. Moderate yellow discharge for two weeks. April 5, 1934, cervix smooth, several nabothian follicle cysts. Uterus anterior, slightly enlarged, slightly irregular, limited mobility, sensitive. Adnexa right side, enlarged, adherent to posterior broad ligament, dropped into culdesac and adherent to floor of pelvis. Left side, enlarged, extends laterally for some distance and adherent to posterior broad ligament. About four inches in diameter. Parametrium markedly infiltrated posteriorly. Diagnosis: Bilateral salpingo-oophoritis, pelvic cellulitis. She had 7 treatments from April 14 to May 1, 1934. April 21, sweating, flushing, salivation, slight fall in blood pressure during treatment. Adnexal and parametrial exudate almost completely dissipated. On May 1 tubes and ovaries and parametrium entirely negative. June 21, no treatment for seven weeks. No complaints. Cervix smooth, few nabothian follicle cysts, no discharge. Uterus tipped to the right and drawn back. Right ovary small and palpable. Right tube negative. Left tube and ovary negative.

Comment: This patient had an exacerbation of a previous tubal inflammation. The exudate entirely disappeared after sixteen days of treatment.

Case 8.—(A84274) G. H., twenty-one years of age, married two years, no children, one abortion induced four years ago followed by fever, menstruation regular, one week profuse, painful. Moderate yellow discharge and pain in the lower abdomen for one year. Cervix small. Uterus anterior and small, fixed, drawn back into the hollow of the sacrum. Adnexa, right tube thickened, right ovary palpable, prolapsed. Left tube markedly enlarged. Left ovary large. Parametrium thickened posteriorly and laterally. Bilateral salpingo-oophoritis, parametritis. She had 14 treatments from May 12 to June 23, 1934. After the seventh treatment the tubal involvement practically disappeared. Both ovaries palpable. Had an exacerbation lasting two days following swimming. June 23, 1934, right tube negative. Right ovary palpable. Left tube negative. Left ovary enlarged, irregular, small cystic degeneration.

Comment: This patient had an exacerbation of a preexisting infection. The inflammatory exudate disappeared in nineteen days. Treatment was continued for twenty-three days without additional effect on the ovarian enlargement.

Case 9.—(A83929) C. M., forty-five years of age, married twenty years, 5 children, youngest seven years old, two miscarriages, last one five years ago, menstruation regular, one week, profuse. Pain in lower abdomen seven months. Vagina relaxed. Cervix hard. Uterus not distinctly outlined, incorporated with masses on either side. Right side filled with a mass extending to the pelvic wall about five inches in diameter. Firm and immobile. Left side smaller mass somewhat softer in consistency, tender. Tuboovarian inflammation. She had 8 treatments from April 17

to May 8, 1934. On May 3, 1934, mass on left side about 1.5 inches in length, sensitive. Uterus tipped to right and adherent. Mass on right side extending to the posterior pelvic wall and behind uterus and holding the uterus fixed. May 8, uterus enlarged, hard, and irregular. Tipped to the right and adherent. On the left side large cystic mass about three inches in diameter, slightly movable. Diagnosis: Now changed to fibroid uterus. Right adnexitis. Left ovarian cyst. Admitted to hospital for operation. Operated upon May 11. Liberation of adhesions, supravaginal hysterectomy, bilateral salpingo-oophorectomy. Operative diagnosis: Adhesive peritonitis. Chronic pelvic cellulitis. Dermoid cyst, left ovary. Intraligamentous cyst, right ovary. Wound dehiscence developed on third day. Paralytic ileus. Heostomy performed. Patient died in twenty-four hours.

Comment: This patient had a bilateral cystic degeneration of the ovaries with a surrounding inflammation of the pelvic peritoneum. Local treatment for twenty-one days failed to affect the pelvic masses. Operation disclosed the cystic degeneration of the ovaries.

Case 10.—(A86403) F. G., thirty-five years of age, married eight years, divorced seven years, no children, menses regular, three to four days, painful. Pain in both lower quadrants, two weeks. Backaches past two weeks. Discharge slight. Fever 103° F. Was admitted to the hospital on May 15, 1934. Pelvic floor negative. Vagina negative. Cervix negative. Uterus not definitely made out, large mass to left filling pelvis and extending down into culdesac. Similar mass to right, firm, fixed, tender. Bilateral salpingo-oophoritis. Blood count, 18,850 white blood corpuscles, 90 per cent polynuclear leucocytes. Sedimentation time eight minutes. Temperature ranged between 99° and 103° F. with daily rise for eight days, then became normal and remained so for the next seven days. Had six treatments while in hospital, the treatments being given regardless of temperature. Discharged from hospital May 29. Treatments were continued in the clinic. She received 22 treatments up to July 19, 1934. Elapsed time, sixty-four days. During the course of the treatment a cessation of progress was noted after about ten treatments. The remaining treatments were given to determine what further changes would occur. July 14, the pain in the abdomen and backache disappeared. The painful menstruation was considerably relieved. Uterus moderately movable. Mass on left side, easily defined about four inches in diameter, distinctly cystic, fixed. Right side no palpable pathology. Diagnosis at this examination, ovarian cyst, left, adherent. The similarity of this condition to that of Patient 9 is striking both as to the original pathologic alterations and the subsequent course under treatment, Case 9 the presence of the ovarian cyst was proved.

Comment: In this patient the inflammatory exudate was apparently absorbed, and the failure of further recession of the mass and its distinctly cystic character make the diagnosis of adherent ovarian cyst most probable. The relief of symptoms was the result of disappearance of the active inflammatory process.

DISCUSSION AND SUMMARY

An effort was made to determine whether the physiologic action of acetyl-beta-methylcholine-chloride could be produced in the pelvis. From the physiologic effects produced on the skin, it seemed reasonable to expect that the prolonged vascular dilatation and the stimulation of circulation would exercise a powerful influence in promoting the absorption of an inflammatory exudate.

The results in the first patient treated were encouraging. There was, however, no large amount of exudate present, and although the painful menstruation and lower abdominal pain were relieved, the patient still

complained of pains elsewhere. This constituted an uncertain clinical picture.

The next five patients had huge inflammatory exudates in the cellular tissues and tubes. The rapidity with which the exudates disappeared under treatment was astonishing and justified its continuation.

In the seventh patient the first indication of limitation of effect was noted. There was an old cervicitis with many nabothian follicle cysts, in addition to the acute flare-up in the cellular tissue and tubes. Two months after the complete disappearance of the pelvic exudate, the nabothian cysts were still unaffected.

The eighth patient added another condition which was not influenced by the treatment. After the disappearance of the tubal and parametrial exudate, the left ovary, which had become distinctly palpable, enlarged, and presented small cystic degeneration, failed to diminish in size. After several additional treatments had been given, it was apparent that no change would occur, so treatment was discontinued.

In the ninth patient, the first positive evidence of the limitation of effect was obtained. Treatment was begun for what was thought to be a pelvic inflammation. After several treatments, with practically no change in the size of masses, but with more discrete delineation, it was believed that the mass at least on one side was cystic. At operation, both lateral enlargements proved to be ovarian cysts.

The pathologic condition in the tenth patient was similar to that in the previous one. This patient was given additional treatment to see what effect, if any, repeated applications would have. Practically no change in the pelvic condition was observed.

Of the ten patients treated by the iontophoresis of acetyl-beta-methyl-choline-chloride, seven, with extensive pelvic inflammation, were completely cured. In several, concomitant painful menstruation was relieved. No effect was produced on nabothian follicle cysts, small cystic degeneration of the ovaries, or large ovarian cysts. Further investigations to more completely define the uses and limitations of this treatment are in progress. So far as one can judge from a small number of cases, it is likely that this method of treatment is an effective agent in promoting the rapid absorption of inflammatory pelvic exudates, with incidental relief of symptoms. It produces no change in productive pathologic conditions. It seems to be superior in its effects to other methods of exciting pelvic hyperemia because it has a much more sustained physiologic action.

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¹⁵¹ WEST 77TH STREET

A RÉSUMÉ OF 223 CASES OF SURGICAL STERILIZATION*

CLIFFORD B. LULL, M.D., PHILADELPHIA, PA.

A DISCUSSION of the problems involved in the sterilization of human beings brings up so many controversial subjects that I approach my topic with the full realization of these varied angles, and with the intention of not entering too deeply into their discussion.

During the past few years we have had before us continually, because of laws passed in various countries, the very grave and serious problem of sterilization for eugenic or economic reasons. It is not my purpose to discuss this phase of the subject, but one can hardly write of sterilization that this does not come to the front. It is mentioned here because there are a few patients in this series where the economic and eugenic problems unquestionably influenced our decision to perform the operation, not as a primary factor, but secondary to what we considered a medical problem. As there are so many debatable sides to this question at the present time, I feel that, unless one is practicing in a commonwealth where definite statutes can be clearly interpreted as to what constitutes the mental defective or the psychopathic inferior, and until it is definitely settled just what are the constitutional rights of a person living in these days of political upheaval, these problems had better not be pushed too far. When our Supreme Court has difficulty in deciding whether or not the constitution of these United States has been tampered with, and until there is more definite crystallization of opinions on this subject, I can only see many complications arising from enforced mass sterilization. The English legal position, summed up, says sterilization for reasons of health is always lawful; for eugenic reasons, probably unlawful; in lunatics, always unlawful except for health reasons. How much longer it will be before more radical laws will be passed in England, or how soon this issue will be decided in our own country. I do not know; but I believe that the medical profession must enter into the discussion of these problems more actively and take a definite stand in these matters. Therefore, that which confronts those of us practicing obstetrics and gynecology in a commonwealth where there are no laws as far as eugenic sterilization is concerned, is the problem of relieving suffering individuals or prolonging their lives, where in our opinion a continuation of childbearing would be harmful. This is particularly true in the more ignorant type of patient, because on several occasions I have found permission for the operation signed by the patient and hus-

^{*}Read by invitation at a meeting of the New York Obstetrical Society, May 14, 1935.

band, and upon investigation, have discovered that an overzealous interne had gotten permission for operation, but the patient had not understood. One must also be circumspect where religious beliefs are opposed to the operation.

We are all familiar with the fact that at times statistics cannot be depended upon, but up to the present time we have no other means of knowing accurately what our end-results are. It has been our custom at the Philadelphia Lying-In Hospital to check accurately, statistics on various procedures from time to time in order to be sure that our results are as satisfactory as we believe them to be. It is my purpose, therefore, to show to you, very briefly, our statistics on those patients upon whom we thought it advisable to perform sterilization operation.

RÉSUMÉ OF STERILIZATIONS

Of 17,130 admissions to the Philadelphia Lying-In Hospital from Oct. 1, 1924 to Dec. 31, 1933 (nine years, three months), there were: Obstetrical cases, 14,038 or 81.94 per cent, and gynecological cases, 3,092 or 18.05 per cent.

Of the total 17,130 cases admitted, 223 or 1.30 per cent were sterilized: At cesarean 111 or 0.64 per cent, at hysterotomy 19 or 0.11 per cent, and at gynecologic operation 93 or 0.54 per cent.

Of the 223 patients sterilized: 155 or 69.5 per cent, answered no to questionnaire (no future pregnancies after sterilization); 5 or 2.2 per cent died; 63 or 28.2 per cent, letters returned or no answer.

The patients' ages ranged from fifteen to forty-four, the average age being thirty. The parity ranged from one to seventeen, the average, 3.7. The religion included Protestant 106, Catholic 53, Jewish 7, Quaker 1, Greek 1, and unknown 55.

Indications for sterilization were as follows: Cesarean section: second section 53, third section 11, toxemia 13, cardiac 13, renal 3, severe varicose veins 1, difficult labors 2, active tuberculosis 1, psychiatric cases 2, sclerosed cervix 1, suspension at previous operation 1, placenta previa, para vi, poor health 2, epilepsy 1, first pregnancy nineteen years ago 1, phlebitis 1, hyperneurosis 1, previous plastic 3, and para vii, forty-three years, premature separation 1.

Indications for sterilization at hysterotomy: Toxemia 6, cardiac 5, renal 2, hyperneurosis 1, multiple myomas, gastric ulcer 1, tuberculosis 2, diabetes 1, and epilepsy 1.

Indications for sterilization at gynecologic operation: Laceration of cervix, laceration of pelvic floor and prolapse 85, toxemia, para x 1, cardiac 2, extensive plastic 1, ovarian cyst, para iii, poor health 1, left tubal pregnancy, ruptured 1, right ovarian cyst, prolapse, varicose veins broad ligament 1, and Parkinsonian disease 1.

Anesthesia: Gas-ether 159, ether 31, spinal 2, local 20, novocaine, gas and oxygen 3, nitrous oxide and oxygen 6, chloroform 1, and ether and novocaine 1.

Causes of morbidity (147): Postoperative reaction 94, pulmonary infections 13, urinary tract infections 7, myocarditis 2, sapremia and endometritis 13, wound infection 5, breast abscess 1, peritonitis 1, pelvic abscess 1, diabetic complication 1, emotional reaction 1, gastrointestinal upset 4, dehydration 1, postoperative cervical hemorrhage 1, and phlebitis 2.

In 223 cases there were 5 or 2.24 per cent adult deaths: Nephritic toxemia 1, pulmonary embolism 1, acute myocardial failure 1, peritonitis, premature separation 1, and lobar pneumonia 1. The nephritic toxemia was an emergency case which did not respond to treatment. Pulmonary embolism occurred thirteen days following operation

for prolapsus. The acute myocardial failure occurred four days following cesarean section for premature separation. Sterilization was done because of the cardiac condition. Peritonitis occurred following cesarean section which was done for premature separation. Classical section was done as this patient had had no examinations and membranes were intact. Sterilization was performed because of her cardiac condition. The pneumonia developed following cesarean section under local anesthesia. This patient was referred to us for cesarean section and sterilization by the cardiovascular clinic.

METHODS OF STERILIZATION

At the present writing there are several methods of sterilization in the female. As these statistics have only to do with surgical procedures, I shall omit all discussion on sterilization by irradiation, radium, hormonal sterilization, spermotoxins, or other procedures which have been advised from time to time.

In the discussion of sterilization by surgical methods, I believe that in the absence of pathology in the uterus or in the ovarian structure, the removal of these organs to prevent conception should not be done, particularly in women during the second and third decades of life. It, therefore, narrows our discussion to operative procedures which produce anatomic changes that will keep the spermatozoa from meeting and fertilizing the ovum. It furthermore practically narrows down to operations upon the fallopian tubes.

When one consults the literature as to the best method of obtaining this result, one is impressed first, by the innumerable procedures which have been advised, and second, by the fact that in almost every method where a large series has been reported there has occurred a failure. I shall not take time to enumerate or discuss the various procedures which have been advised, but will concentrate my discussion on the method which has been employed in this series of 223 cases. The same procedure has been carried out in each case.

Up until October, 1924, we had no standardized method of sterilization. The general rule, however, was to remove both fallopian tubes with a wedge-shaped piece of the cornu of the uterus. Shortly before this time we were particularly impressed by two things; one was that notwithstanding the supposedly complete removal of the cornual end of the tube, one or two patients became pregnant; and second, there were, within a short period of time, five patients admitted who had to have subsequent laparotomies because of cystic disease of one or both ovaries following salpingectomy. From the clinic of the late Dr. Ralph Pomeroy, there emanated a technic for operation upon the fallopian tube which, because of its simplicity and safety, warranted a trial. We were not at all impressed with its security, but as time went on we have become more and more impressed with the fact that it might be described as not only safe and simple, but also a secure procedure. Although I do not believe that Dr. Ralph Pomeroy made

any claim for its originality, we have used his name in connection with this operation, and on our records it is known only as the Pomeroy operation.

The procedure consists simply in picking up the middle portion of each fallopian tube, ligating it with an absorbable suture and then resecting the loop. The importance of using an absorbable suture cannot be stressed too much, because when one uses a silk ligature the chances of fistula formation are unquestionably increased. Practically no bleeding occurs, although when doing this by the vaginal route some tearing of the mesosalpinx may occur and give rise to moderate hemorrhage. I have never seen hemorrhage in doing this operation by the abdominal route which required any extensive ligation or resection of the tube. At subsequent laparotomy upon four of the patients in this series, it was definitely demonstrated that the cut ends had drawn apart and that the plastic exudate of the peritoneum had become organized in such a manner that it did not seem possible for a fistula to occur. Both ends of the tubes were shrunk up to a very narrow strand. In addition to having the opportunity of studying these cases at subsequent operation, we have injected lipiodol into the uterine cavity of many of them. In no case was there any escape of lipiodol from the uterine cavity.

I have heard some criticism of this very simple operation. In fact I have seen the sections from a patient who afterward became pregnant, and was particularly impressed with the fact that it was necessary to cut '1,300 serial sections before the tubal lumen could be demonstrated. I would be of the opinion that in this particular case the spermatozoa were endowed with unusual persistency and vitality. Furthermore, I have operated upon one patient who had the right fallopian tube resected and the left round ligament. Unquestionably it is necessary to do this operation on both fallopian tubes for it to be successful. We do not feel at the present time that this operation may not at some time in the future be a failure in one or more cases, but in this rather large series it has proved so satisfactory that we believe we shall continue to use it until it has been proved otherwise.

Bishop and Nelms in 1930 reported a hundred patients sterilized by this method with no known subsequent pregnancy. In their paper they have summarized the results of the various other tubal procedures in practically all of which there was a fairly high percentage of pregnancies following the operation. It is only by adding statistics to the literature that we may eventually come to some conclusion as to what is really the best method of operating upon the fallopian tube to prevent impregnation. I believe that the two important steps in this operation are not to crush the tube, and the use of an absorbable suture. If I could find in the literature at the present time statistics showing a lower incidence of failures than have occurred in our own series, I should be perfectly willing to change this method; until, however, I have actually had in my own service, or have seen reported by other individuals, these statistics, I feel that the simplicity and safety of this operation warrants its continued use.

SUMMARY

- 1. A series of 223 patients operated upon by the Pomeroy method of sterilization is hereby reported.
- 2. This number of 223 patients constituted 1.30 per cent of all patients admitted to the Philadelphia Lying-In Hospital on both obstetric and gynecologic services from Oct. 1, 1924, to Dec. 31, 1933, a period of nine years and three months.
 - 3. A definite follow-up was obtained in 71.7 per cent.
 - 4. All patients in this series were sterilized by the same method.
- 5. Because of its simplicity and safety, and because there have been no known failures up to the present time, we feel that it is also a secure operation to do.
 - 6. This operation can be done vaginally as well as abdominally.
- 7. Five deaths occurred in this series; all were either bad operative risks or death was caused by some of the accidents of postoperative convalescence.

Finally, this series is reported to stimulate similar evaluations of results in other clinics. In the light of our experience with this procedure, together with a review of the results of other methods, we believe that the simplicity and safety of the Pomeroy operation warrants its continued use.

1731 PINE STREET

Doan, R. C., and Simpson, W. M.: The Elliott Treatment of Pelvic Inflammatory Disease, Am. J. Surg. 28: 78, 1935.

In a series of 101 cases of pelvic inflammatory disease, good results were obtained in 67 per cent, fair results in 25 per cent and poor results in 8 per cent. Satisfactory improvement was noted in 92 per cent of the cases. In a group of 52 cases, including chronic salpingitis, acute exacerbation of chronic salpingitis, acute and subacute salpingitis, good results were obtained in 67 per cent, fair results in 23 per cent and poor results in 10 per cent. Satisfactory results were observed in 90 per cent of this group.

The highest proportion of good results was found in the acute and subacute forms of the disease with duration of less than three months. The erythrocyte sedimentation rate was found to be a reliable index of the resolution of the inflammatory process in approximately two-thirds of a group of 77 patients.

Gonococci disappeared from the cervical smears of all but 1 of 12 adult patients. Gonococcal vaginitis of children was found to be refractory to Elliott therapy in 3 of 4 cases.

The authors suggest that approximately 9 out of 10 patients with pelvic inflammatory disease may be treated successfully with Elliott therapy, without recourse to surgical intervention. In the few cases in which complications make surgery necessary, Elliott therapy before and after operation will greatly enhance the likelihood of prompt and favorable results.

J. THORNWELL WITHERSPOON.

THE MONTH OF CONCEPTION OF 935 CONGENITALLY MALFORMED INDIVIDUALS

Douglas P. Murphy, M.D., Philadelphia, Pa.

(From the Gynecean Hospital Institute of Gynecologic Research and Department of Obstetrics and Gynecology, University of Pennsylvania)

INTRODUCTION

FOR the City of Chicago, Petersen has found a greater frequency of conceptions of congenitally malformed individuals during the months of March and April (120 per cent of expectancy), than in July, August, and September. Throughout the spring months, he also notes a greater variability in barometric pressures than during the summer season.

Believing that human protoplasm is more unstable in spring than in summer, he suggests that there may be a cause and effect relationship between the spring variations in barometric pressures and the unusually high conception rate of malformed children observed by him at that time.

Recently, the month of conception of 935 congenitally malformed children born in the City of Philadelphia was determined. This information is of interest in the light of Petersen's conclusions.

MATERIALS AND METHODS

To quote from a previous communication,² the material forming the basis of this report was collected in the following manner:

"There were found in the files of the Bureau of Vital Statistics, Department of Health of the Commonwealth of Pennsylvania, 130,132 death certificates for all stillborn and liveborn individuals who died in Philadelphia during the five-year period between Jan. 1, 1929 and Dec. 31, 1933. Each of these certificates was examined, and the data on those noting the existence of any congenital defect were transcribed to duplicate, official forms. Fourteen hundred and seventy-six such certificates were located.

The deceased individual was considered to have possessed a defect under either of two conditions: (1) If the defect involved the surface of the body, or (2) if internal, its presence had been disclosed by operation or necropsy. Diagnoses not conforming to these requirements were considered as not verified and were excluded from further consideration. This procedure reduced the number of usable certificates to 890, or only 60 per cent of the original 1,476 certificates.

Birth certificates for 90 per cent of the 890 defective individuals for whom death certificates were available also were located.

An attempt was made to interview the mother of each of the 890 deceased individuals, the visits being made in the summer of 1934 by 3 fourth-year medical students. A complete reproductive history was secured from each mother that could be located-which included data upon the month of conception of all pregnancies. More than 540 mothers were interviewed.

The facts found in: (a) the birth and death certificates of the 890 defective children, and (b) the information secured from the mothers. gave data for the month of conception of 2,525 offspring.

Some of the 2,525 pregnancies ended in abortion or miscarriage. The embryos in such cases were considered to have been normally developed unless there was definite information to the contrary.

The 2,525 individuals included 1,590 normally developed children, and 935 that were known to be congenitally malformed. Of the 935 defective children, 45 were discovered as a result of the home visitation. Most of these were dead, though 17 were still alive at the time that the home visits were made.

RESULTS

The malformations met with in the 935 defective children are classified in Table I; in more than 75 per cent of cases, the defect involved the body surface.

TABLE I. CHIEF DIAGNOSIS OF EACH CONGENITALLY MALFORMED INDIVIDUAL

A classification of the defects of the congenitally malformed individuals for whom month of conception was determined. Each person assigned a single diagnosis, the latter being the most severe one in cases where two or more defects were present.

OHOMBA	INDIVIDUALS		
SYSTEM	NUMBER	PER CENT	
Reported	935	100.0	
Nervous	567	60.7	
Gastrointestinal	139	14.9	
Cutaneo-musculo-skeletal	103	11.0	
Cardio-vascular	80	8.5	
Monsters not described	28	3.0	
Urinary	10	1.1	
Respiratory	3	0.3	
Ill-defined	5	0.5	

That the defects in most instances were serious is indicated by the ages of the defective children at the time of death. Of the 935 malformed individuals, 233 (24.9 per cent) were stillborn; 586 (63.5 per cent) died under one year of age; 98 (10.0 per cent) died after one year of age. In one case, the age was unstated, and only 17 defective individuals were living at the time that the study was made.

The months of conception of the 935 defective persons and of their 1,590 normally developed siblings are compared in Table II, where their percentage frequency of occurrence is also shown. The latter percentages are expressed graphically in Fig. 1. Here the horizontal line, marked "N," represents the percentage frequency of distribution of all of the conceptions of both defective and normal individuals, had they been equally distributed throughout the twelve months of the year.

From these data, it appears that these defective individuals born in Philadelphia were not conceived most often in the months of March and April as found by Petersen, but in the months of June, July, and August, the time at which he noted the least frequency of occurrence. And, as shown in Fig. 1, the normal siblings of the defective individuals were conceived most often in the spring months and least often in the summer months.

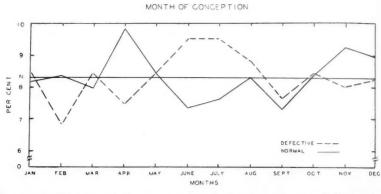
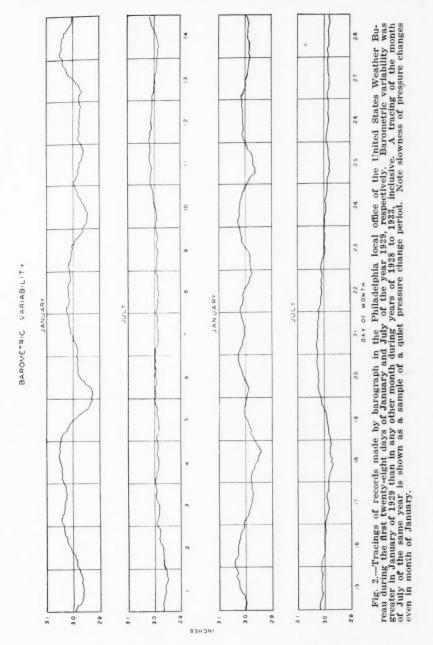


Fig. 1.—Showing the month of conception of: (a) the 935 congenitally malformed individuals, and (b) 1,590 of their normally developed siblings. Data are taken from columns 3 and 5, Table II. Base line represents months. Vertical line records percentage distribution. Line "N" represents the percentage distribution, had the 2,525 conceptions been evenly distributed throughout the twelve months. Note the greater frequency of conception of malformed individuals in the summer months, and of the normal individuals in the spring and fall months.

TABLE II. MONTH OF CONCEPTION OF CONGENITALLY MALFORMED CHILDREN AND OF THEIR NORMALLY DEVELOPED SIBLINGS

MONTH	CONCEPTIONS				
	DEFECTIVE		NOB	RMAL	
	NUMBER	PER CENT	NUMBER	PER CENT	
(1)	(2)	(3)	(4)	(5)	
Jan.	79	8.45	130	8.18	
Feb.	64	6.34	133	8.36	
Mar.	79	8.45	127	7.99	
Apr.	70	7.49	157	9.88	
May	79	8.45	134	8.43	
June	89	9.52	117	7.36	
July	89	9.52	121	7.61	
Aug.	83	8.88	132	8.30	
Sept.	72	7.69	116	7.30	
Oct.	79	8.45	133	8.36	
Nov.	75	8.02	147	9.24	
Dec.	77	8.24	143	8.99	
Totals	935	100.00	1590	100.00	

Chartometer measurements of the barographic records made in the Philadelphia local office of the United States Weather Bureau during



the years 1928 to 1933, inclusive, indicate that in this region, the greatest barometric variability is met with in January, and the period of least variability in June, July, and August.

From a study of the above records, the month of January of the year 1929 was found to exhibit the greatest degree of barometric variability. A tracing of the record of the first twenty-eight days of this month is reproduced in Fig. 2, where it can be compared with a similar tracing for the month of July of the same year. These two tracings indicate the differences in barometric variability observed in these months in the region of Philadelphia.

DISCUSSION

From the available data, I am unable to find any significant, seasonal incidence of the conception of congenitally malformed individuals in Philadelphia. Nor am I able to correlate the conception rate of defective persons with the rate of change of barometric pressures. That I cannot confirm the findings of Petersen may possibly be due to differences in barometric conditions as met with in Chicago and Philadelphia.

Changes in pressure in the latter city, however, even during periods of greatest variability, are slow, as indicated by the record portrayed in Fig. 2. The slowness with which the most rapid changes occur in Philadelphia makes it difficult to believe that they can influence the development of the human embryo in utero. Unless the pressure changes in other places are considerably more rapid than in Philadelphia, it does not seem likely that they play any rôle in influencing the conception rate of congenitally malformed individuals. If a preponderance of such conceptions does take place at certain seasons of the year, in other localities than Chicago, other factors than barometric pressure changes and weather conditions may have to be ruled out before a final decision can be made in favor of the weather. Future reports by observers in other places are awaited with interest.

SUMMARY AND CONCLUSIONS

- 1. Data are presented on the month of conception of 935 congenitally malformed children who died in Philadelphia during the five-year period between Jan. 1, 1929, and Dec. 31, 1933, and concerning the month of conception of 1,590 of their normally developed siblings.
- 2. More than 90 per cent of the defective individuals were born in Philadelphia, and approximately an equal proportion died within a year of birth.
- 3. No evidence can be found to support the view that in Philadelphia there exists any significant, seasonal trend toward the conception of congenitally malformed children.

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IS THE OVAL OR FEMALE TYPE PELVIS A RACHITIC MANIFESTATION?

Herbert Thoms, M.D., New Haven, Conn.

(From the Department of Obstetrics and Gynecology, Yale University School of Medicine)

In a recent communication I discussed the question "What Is a Normal Pelvis?" and pointed out that our recent knowledge of pelvic variations has shown that the occurrence of the oval or female type pelvis in women is by no means as great as hitherto supposed. In a recent study I demonstrated that in 135 consecutive primiparous patients this type occurred in but 51.8 per cent, while the round and anthropoid types occurred in 48.2 per cent of the series. This corresponds with the findings of Caldwell, Moloy, and D'Esopo² who, in a series of 215 cases, found the gynecoid or female type in 53.9 per cent.

In the communication first referred to I suggested that the oval or female type pelvis might in reality be a result of mild rachitis occurring in early childhood or at puberty. To quote; "the predominant type of pelvis which was formerly seen in clinics may have actually changed in character within a generation. When alterations are considered in environment surrounding female infants and adolescent children during the past twenty-five years, changes brought about not only by a great difference in diet, but by such influences as outdoor exercise and life in the open, it must be admitted that the environment for this group has changed indeed during that period. When one further considers the sedentary habits, the type of clothing, the diet, and general restrictions that previously were a part of the life of female infants and children, may one not speculate as to the effect of such an environment on the adult form of the female pelvis. That changes in environment can effect skeletal changes in a large proportion of a population is witnessed in recent years by the extraordinary lessening of the incidence in children of severe rachitis." In this communication also I mentioned the suggestions of Stoney³ and Vaughan⁴ that oval pelves are not truly the result of racial influence but are caused by conditions of life in modern civilization. I wish again to quote Hess⁵ and his associates who state that "Although the incidence and severity of rickets in the United States has decreased in the last five or ten years, it must not be thought that it has become a negligible disorder. A clinical survey of rickets which we carried out this winter (1930-1931 in New York City) among the poor who

attended health stations showed that fully half the white infants and approximately three-fourths of the negro infants have definite signs of rickets."

The present communication is based on a study of the pubic and iliac portions of the line of "terminal length" in the pelves of fifty women and in order to make the study somewhat clearer I may briefly outline the "Terminal Length" theory of Breus and Kolisko.6 These authors maintain that the relative flattening of the superior strait in the adult pelvis is due not so much to mechanical forces but to differences in rate of growth before puberty of certain portions of the pelvic bones. They pronounce particular importance upon the socalled terminal length of the innominate bone. They point out that if we saw through the innominate bone at the level of the iliopectineal line and view the sawn surface of the upper half, we shall see that the surface may be arbitrarily divided into three parts, the sacral, iliae. and pubic portions. These are practically of equal length, the whole being in the neighborhood of 20 cm. In the period of development these portions arise from the following, the sacral portion from the cartilage of the iliac crest, the iliac portion from the Y-shaped cartilage of the acetabulum and the pubic portion from the same cartilage and from that of the symphysis. These authors contend that the variations in the rate of growth of these three portions are the most important factors in determining the shape of the pelvis and that mechanical factors play a distinctly minor rôle.

They further state that in rachitis the pubic portion retains its normal proportions, the iliac portion being greatly shortened and the sacral portion slightly shortened. When this change is present, they state that it is almost pathognomonic of rachitis.

With these facts in mind it occurred to me that a study of terminal length components, particularly the pubic and iliac portions in the female, round and anthropoid types of pelvis might show something of interest. Accordingly, twenty-five female type pelves and twenty-five round-and anthropoid type pelves were studied by roentgen pelvimetry, with results shown in Tables I and II.

In surveying the tables it will be noted that in the "female type series" the difference between the length of the pubic and iliac portions of the terminal length is far greater than that in the "round and anthropoid series." In nearly all instances the iliac portion is from 1.0 to 2.25 cm. shorter than the pubic portion.

It might be well to state that in studying the roentgenograms of the superior strait in both series, the point at which the shadow of the acetabulum makes its nearest approach to the iliopectineal line, was chosen as the junction of the pubic and iliac portions, the center of the symphysis pubis and the shadow of the sacroiliac articulation

TABLE I. FEMALE TYPE SERIES

CASE ANT. PO	SUPERIOR STRAIT				
	ANT. POST. DIAM.	TRANSVERSE DIAM.	PUBIC POR-	ILIAC POR-	DIFFERENCE
1	11.25	13.25	7.5	5.75	-1.75
	11.25	13.5	7.5	6.5	-1.0
2 3	10.25	12.0	7.25	5.5	-1.75
4	9.75	11.75	6.75	5.25	-1.5
5	11.5	13.75	8.25	6.0	-2.25
6	11.5	13.5	8.25	6.0	-2.25
7	10.5	13.5	7.25	5.75	-1.5
8	10.5	12.5	7.0	6.0	-1.0
9	11.5	13.0	7.75	6.0	-1.25
10	11.0	13.25	7.5	6.25	-1.25
11	10.25	13.00	8.0	5.5	-2.5
12	9.75	12.25	7.25	5.25	-2.0
13	10.75	12.75	8.00	5.75	-2.25
14	11.25	13.5	7.75	6.75	-1.0
15	12.0	14.0	8.25	7.0	-1.25
16	11.0	13.25	7.75	6.5	-1.25
17	11.25	13.5	7.75	6.75	-1.0
18	11.0	12.5	7.75	5.50	-2.25
19	9.75	12.0	6.25	5.5	-0.75
20	11.25	13.0	7.75	6.0	-1.75
21	11.5	13.75	8.5	6.25	-2.25
22	10.75	13.5	7.0	6.25	-0.75
23	11.5	13.5	8.0	6.25	-1.75
24	11.5	14.25	7.25	6.5	-0.75
25	11.0	13.0	7.5	6.25	-1.25

TABLE II. ROUND AND ANTHROPOID SERIES

CASE SUPERI ANT. POST. DIAM.	SUPERIOR STRAIT		PUBIC POR-	ILIAC POR-	DIFFERENCE
	MAI, TOBI. INAMSVERSE				
1	12.75	13.25	7.75	7.75	0.0
2	11.5	11.75	6.5	6.5	0.0
3	12.0	12.0	6.75	6.5	-0.25
4	12.75	12.75	7.25	7.0	-0.25
5	11.5	12.25	7.0	6.75	-0.25
6	12.5	12.75	7.25	7.0	-0.25
7 8	12.0	12.0	7.5	7.0	-0.5
8	12.25	13.0	7.0	7.0	0.0
9	11.75	12.25	7.0	6.5	-0.5
10	12.0	12.5	7.0	7.0	0.0
11	12.0	13.0	7.25	7.25	0.0
12	10.75	11.0	6.75	6.5	-0.25
13	11.5	11.5	6.5	6.5	0.0
14	11.75	12.75	7.0	6.75	-0.25
15	10.0	10.75	6.0	5.75	-0.25
16	10.5	11.25	6.75	6.5	-0.25
17	14.0	12.25	7.75	7.75	0.0
18	13.0	12.0	7.25	7.0	-0.25
19	10.75	10.25	6.25	6.0	-0.25
20	13.0	12.5	7.0	7.0	0.0
21	12.75	12.0	7.0	7.0	0.0
22	14.0	13.25	8.0	8.0	0.0
23	13.5	12.5	7.0	7.0	0.0
24	14.0	13.0	8.0	7.75	-0.25
25	12.5	12.0	7.0	7.0	0.0

being the other end points of these two components. This is illustrated in Fig. 1 and in an illustration from the work of Breus and Kolisko. It becomes evident from this study that in the female type pelvis the

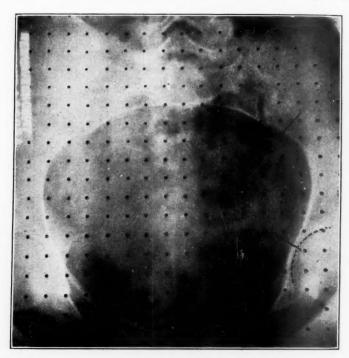


Fig. 1.—Roentgenogram showing division of pubic and iliac portions. Dots represent corrected centimeters in the plane of the superior strait.

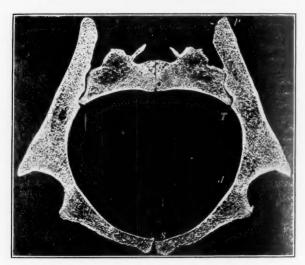


Fig. 2.—Undersurface of superior strait in "female type" pelvis of thirty-six-year-old woman, showing divisions of terminal length; anteroposterior diameter 11.3 cm., transverse diameter 13.5 cm., pubic portion of terminal length 7.8 cm., and iliac portion of terminal length 6.0 cm. (From Breus and Kolisko.)

iliac portion of the line of terminal length is consistently shortened. Whether this is the result of the occurrence of rachitis, probably in a mild form, at some time during the childhood of the individual may be conjectured.

From available information concerning pelves in aboriginal people living in climates in which rachitis does not occur, it appears evident that the round type pelvis is greatly predominant. Furthermore, it seems apparent that the unusual incidence of the round and the anthropoid types in the women of our population must be explained on grounds other than those based on such influences as race and constitution. The above study would appear to be important evidence toward a definite answer to this problem.

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IRRADIATION OF THE PITUITARY GLAND IN THE TREATMENT OF MENOPAUSAL SYMPTOMS

CONRAD G. COLLINS, M.D., M.S., E. PERRY THOMAS, B.A., M.D., AND LEON J. MENVILLE, M.D., NEW ORLEANS, LA.

(From the Hutchinson Memorial Clinic and Departments of Gynecology and Roentgenology, Tulane University, School of Medicine)

THE treatment of neoplastic lesions, commonly occurring at the climacteric, has aroused a tremendous amount of discussion in the literature, and has, rightly, obscured a consideration of the menopausal symptoms, themselves. Hot flushes, sweating, and nervousness, while of no serious moment because they do not harbinger a dangerous condition, are nevertheless quite often of such severity that they cause more discomfort and more true suffering than a serious disease process. Because these symptoms disappear spontaneously later in life and because they, too often, are attributed solely to neurotic origin, they are dismissed by the physician without much consideration. The chief purpose of this paper, containing, as it does, so few cases, is to bring to the attention of the profession a much neglected form of therapeusis in the treatment of the symptoms of the menopause.

The menopausal syndrome is definitely an endocrine disturbance as proved by a multitude of experimental work demonstrating abnormalities which occur in many of the glands of internal secretion at this time.

The frequency and, at times, the sudden appearance of severe menopausal symptoms following castration by surgery or irradiation leads to the logical conclusion that the cessation of ovarian function, accompanied by a withdrawal of the ovarian hormone, is the primary factor in the causation of the condition. This conclusion seems further supported by the relief of these symptoms following the hypodermic or oral administration of the female sex hormone.

However, Tandler and Grosz¹ have shown that castration is followed by an increase in size and function of the anterior portion of the hypophysis; and Rossle² found that the histologic changes accompanying this enlargement, the formation of "castration cells," though not present in all cases, usually required a considerable length of time to make their appearance, but that in some instances, they could be observed as early as four or five days after castration. Engle, confirmed by Evans and Simpson, produced further evidence of the increased activity of the anterior hypophysis, resulting from castration, by implanting anterior pituitary glands from gonectomized rats, showing that these were more potent in stimulating the ovaries of immature animals than was such gland substance from normal rats.

Fluhmann⁵ proved that the same results could be elicited by the injection of blood serum from castrated human beings and that the increased function of the anterior pituitary could be demonstrated as early as eight days or as late as thirteen years after total extirpation of the ovaries; he further demonstrated the failure to obtain these results using blood serum from women with normal menstrual cycles at any time during the cycle.

Changes in other glands, aside from the pituitary have been noted. Tandler and Grosz,⁶ as well as Chouke,⁷ have demonstrated a decreased activity in the thyroid gland at the menopause and this may, in part, account for the accompanying obesity. Hannan⁸ and, similarly, Myers and King⁹ have noted an increased sensitiveness to epinephrine in menopausal women and believe that this occurrence furnishes evidence of a hyperadrenalemia occurring at this time. In no other endocrine organ, however, are the changes so prominent as in the pituitary.

From these facts it appears that the withdrawal of the ovarian hormone simply initiates this endocrine disturbance, known as the menopause, and that the symptoms accompanying it are very probably due to a hyperfunction, or hypofunction, of other endocrine organs in the body, with hyperfunction of the pituitary by far the most noticeable change.

The symptoms of the menopause are chiefly manifested by the occurrence of hot flushes, sweats, increased nervousness, headaches and pains and stiffness in the joints. Usually these symptoms are not severe and the woman, approaching this period, expects some discomfort to accompany her change of life. Occasionally, however, these symptoms become especially severe, particularly from surgical castration, and life becomes miserable for women so bothered. The flushes occur in rapid succession and the sweats in such frequency that the patient is continually bathed in perspiration; headaches become a constant annoyance and aggravate a tendency, already present, to increased nervousness.

It is a time honored custom to treat menopausal symptoms with sedatives and, in the moderate cases, they afford sufficient relief. Cases of greater severity, which are not few in number, exhibit little or no improvement with these measures and are continually seeking relief at the hands of the physician who, too often, has exhausted his resources in the use of bromides and luminal.

Geist and Spielman,¹⁰ Hamblen,¹¹ and Dodds¹² have reported a series of cases in which women suffering from the symptoms of the menopause were treated with injections of the follicular hormone upon the theory that, if the withdrawal of this hormone initiated the symptoms, its replacement should afford relief. Their results might be summarized in the statement that such treatment affords distinct relief in a good number of, but not all, cases; that it is purely substitutional; and that the symptoms return when the administration is discontinued.

Kurzrok¹³ similarly treated a series of women during the menopause with the follicular hormone but divided his cases into two groups. In one group, before treatment, the follicular hormone could be recovered from the urine, while prolan could not be demonstrated, showing the persistence of some ovarian function without hypertrophy of the anterior pituitary. In the second group, the follicular hormone was not present in the urine, whereas prolan was, demonstrating a hyperfunction and hypertrophy of the pituitary and a cessation of ovarian activity. One hundred cases were studied and he concluded that only when the follicular hormone is absent from the urine will relief from menopausal symptoms be obtained by its administration.

The earliest reports of the use of irradiation of the pituitary for the relief of menopausal symptoms are by Groedel¹⁴ in 1922 and by Werner¹⁵ in 1923. The literature covering the subject is small in volume and emanates, almost in its entirety, solely from the continent. Borak^{16, 17} reported a series of fifty cases in 1924 and, in 1929, he reviewed a series of 274 patients, so treated, some of whom had been observed for six years. He reported relief of symptoms in 80 per cent of cases by irradiation of the pituitary alone. In the remaining cases, some improvement followed subsequent irradiation of the thyroid. In 63 per cent of cases, the relief of symptoms lasted longer than six months and from two to four years, while in 27 per cent of cases, the effect lasted less than six months.

To eliminate from his observations the so-called psychic effect of treatment, the one salient argument of critics, Borak interposed a lead screen, sufficient to absorb the rays, between the tube and the patient in a number of cases used as controls. In no case, so controlled, did any change occur in the patients' symptoms. Each of these patients later received a full dose of irradiation, without screening, and relief of symptoms was obtained in every case.

PERSONAL OBSERVATIONS

At the Hutchinson Memorial Clinic, thirty-three patients suffering from menopausal symptoms have been treated by irradiation of the pituitary gland. The technic employed has been the same in all cases.

The irradiation dose for each exposure was 148 r with the following factors: 12 in. D., 5 Ma., 120 K. V. P., 1 Mm. Al and 0.25 Cu, 8 min. The total dosage for each series was 296 r. The first exposure is given through the right temporal region

and on the following day is repeated on the left side; after an interval of approximately three weeks, the same procedure is again performed, making a total series of four exposures, with a total dosage of 592 r to the skin surface. Huet¹⁸ uses a much larger total dosage, and in an experience of three years' duration, he has never failed to obtain relief after a dosage of 2,000 r. No evidence of harmful consequences has occurred.

The symptoms of which these thirty-three women complained were so severe and of such frequent occurrence that they were in a constant state of discomfort and had sought relief from several sources without avail. Every one of these patients had been previously treated with sedatives such as luminal and bromides, and several had received injections of theelin. The failure of these substances to control their symptoms first tempted us to try irradiation of the pituitary gland. The results were so striking in the first few cases that this method has been continued and is employed in all women suffering from menopausal symptoms who experience no alleviation with the use of sedatives.

Only one of our cases, a young woman suffering from a surgical menopause of several years' duration, failed to improve. This patient, when first seen, showed evidences of marked mental deterioration and had been diagnosed as dementia precox by the psychiatry department. Irradiation was attempted chiefly from curiosity to see if any effect could be noticed in this instance. We do not feel that any correct observations can be drawn from this case.

In all of the remaining women, the flushes, sweats, and headaches have decreased in severity and in frequency of occurrence to the point where they are no longer objectionable and, in a good number of cases, have entirely ceased. The nervousness has markedly improved and pains and stiffness in the joints accompanying the menopause have been relieved.

In seventeen of these cases, the menopause had been surgically induced and, in sixteen, it was of natural occurrence. The shortest length of time after irradiation in which improvement was noted has been one week from the first exposure and the longest period to elapse before symptoms were relieved has been six weeks from the first exposure. Improvement is most often noted during the third week of treatment and all patients, except two, have obtained complete relief by the end of three weeks from the last exposure. Two women had obtained only partial relief at the expiration of this time and the flushes and other symptoms, though improved, were still objectionable. In these two cases, two exposures, or one-half of a series, were repeated and relief was promptly obtained. At present, nine months is the longest period of observation for any of these patients; no patients during this period have exhibited a return of their former symptoms or a decrease in the amount of comfort which they had obtained.

In analyzing these cases for this report, it has occurred to us that perhaps the symptoms of the menopause are most probably produced by the excessive amount of prolan secreted by the hypertrophied anterior lobe of the pituitary, and not due to the withdrawal of the female sex hormone, which simply initiates an endocrine disturbance of which the hyperfunction of the pituitary is the chief manifestation. The fact that relief from menopausal symptoms can be obtained by the administration of the female sex hormone is perfectly compatible with this supposition. Wolff, ¹⁹ Smith and Engle, ²⁰ Frank, Goldberger, and Spielman²¹ have demonstrated that the concentration of prolan from the anterior pituitary is lowest when the concentration of the female sex hormone

is highest. This has led to the conclusion that estrin, or the female sex hormone, inhibits the secretion of prolan, and this supposition is the basis of Fluhmann's theory of the hormonal mechanism of menstruation. If this be true, injections of estrin cause a decrease in the concentration of prolan and, perhaps, the relief of menopausal symptoms in this manner. This is in perfect accord with the findings of Kurzrok, mentioned above in the use of theelin (estrin) in the treatment of this condition.

The dosage of x-ray used in the treatment of the series of cases herein reported is a destructive dose in our belief and causes a decrease in the concentration of prolan in that manner. Since actual destruction of tissue occurs, the relief afforded is more permanent. If this supposition is true, irradiation of the pituitary should be followed by a disappearance of prolan from the urine. Unfortunately, no hormonal determinations were made upon these patients. In pursuing this view, it is our intention to determine, in the future, the prolan content of the blood and urine both before and after irradiation and in this way to advance additional support to this contention or disprove it altogether.

CONCLUSIONS

- 1. Sedatives, or the follicular hormone, either alone or in combination, will not relieve menopausal symptoms in all cases. Theelin alleviates the majority of these symptoms, but is transient in effect and purely substitutional.
- 2. Irradiation of the pituitary gland for menopausal symptoms affords more marked relief for a longer period of time and with more lasting effect than any other known type of therapy at present used. It should be employed in all cases where relief is not obtained from sedatives or the follicular hormone.
- 3. Pathologic, biologic, and physiologic investigations have shown conclusively that hypertrophy of the anterior portion of the pituitary with increased prolan secretion occurs at the menopause.
- 4. The supposition is advanced that the symptoms of the menopause are directly produced in large part by the hyperfunction of the pituitary initiated by ovarian atrophy or removal.
- 5. An attempt will subsequently be made to demonstrate the fact that the relief of symptoms afforded by irradiation is accompanied by the disappearance of excess prolan and that this is the effect of a destructive dose of roentgen rays to the hypertrophied pituitary.

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NOTE: The authors wish to thank Miss Margaret M. Sanders for her assistance in this work.

NEMBUTAL IN THE TREATMENT OF PREECLAMPSIA AND ECLAMPSIA

JULIAN WALDO ROSS, M.D., WASHINGTON, D. C.

(From the Department of Obstetrics and Gynecology, Howard University School of Medicine and Freedmen's Hospital)

THE management of preeclampsia, heretofore, has comprised, chiefly, the various means of combating the toxemia with the hope that ultimately all would end well. But this method did not include the use of drugs primarily to prevent the onset of convulsions. As a result many cases of preeclampsia have progressed into eclampsia, the convulsive phase which otherwise might have been averted.

A few drugs, however, e.g. morphine, chloroform, chloral hydrate, and magnesium sulphate, have been employed with varying success to control the convulsions in eclampsia; but these have not been without their added dangers to the already damaged organs and tissues. Because of this fact their routine use has been contraindicated more often than not.

Although the pathologic changes in preeclamptic toxemia differ in no wise from those of eclampsia except in degree, the clinical difference to be feared most is the appearance of convulsions. Hence, the need of a drug or drugs which would both prevent and control convulsions and at the same time offer the least insult to an already damaged organism has long been a pressing desideratum.

The treatment of preeclampsia and eclampsia not unlike that of many diseases is both prophylactic and active. The prophylactic treatment of preeclampsia includes preconceptional and prenatal care. With the use of nembutal, the active treatment of the nonconvulsive phases of preeclampsia is a rational prophylactic treatment of eclampsia.

During the past three years, thirty-five cases of preeclampsia were treated with nembutal (0.1 gm. capsules per os, one four times daily)

none of which developed convulsions. Three treated without nembutal developed convulsions.

The following is a typical case. A. W., aged thirty-six, para vi, was admitted to hospital at 11:30 p.m., complaining of cramplike pains every five minutes in the lower back and abdomen and an intermittent watery discharge from the vagina since early morning. Abdomen overdistended, muffling the fetal heart sounds. Interne's impression, preeclampsia, polyhydramnios. Blood pressure 190/130; urine negative; Fouchet test positive; sedimentation rate 30 mm. in forty-five minutes; eyegrounds negative; Wassermann negative; phenolsulphonephthalein test 40 per cent. Diagnosis: Labor at term, polyhydramnios, preeclampsia.

At 12:30 a.m. patient was given three nembutal capsules per os; 1:30 a.m. patient exceedingly restless. At 1:45 patient lapsed into semicomatose state; 2:00 a.m. fetal head presented; 2:10 a.m. an apparently normal live infant born; 5:15 a.m. patient sleeping; 7:00 a.m. patient complained of severe pains in abdomen; 10:00 a.m. two nembutal capsules ordered given per os, b.i.d.; 11:00 a.m. patient drowsy. Thereafter the patient was comfortable; no further complaints. The nembutal was discontinued on the fourth day postpartum. The blood pressure progressively dropped to 110/70. The patient and infant were discharged in good condition on the thirteenth day postpartum. There were no convulsions.

In twenty-four treated cases of eclampsia (twenty-three of which had no prenatal care) the use of nembutal promptly stopped and completely controlled the convulsions; whereas, morphine sulphate given repeatedly failed to do so in two cases. Nembutal was administered either intravenously 0.2 gm. in 4 c.c. normal salt solution followed by six to eight capsules per rectum or ten to twelve capsules, per rectum, only.

The following case is typical of the eclampsias in which nembutal was employed: B. H., aged seventeen, primipara, brought into hospital on stretchers at 1:45 p.m., drowsy, having had one convulsion with loss of consciousness two hours before entering the hospital. Interne's impression, cyesis, eclampsia. Blood pressure 170/120; temperature normal; urine four-plus albumin, sp. gr. 1,021, otherwise negative; Fouchet test negative; sedimentation rate 24 mm. in forty-five minutes; eyegrounds, left eye, negative; opacities in refractive media of right eye prevented observation of fundus; Wassermann negative; no test done for renal function. Diagnosis: pregnancy at term, eclampsia.

At 4:45 p.m. patient had another convulsion lasting three minutes; 5:20 p.m. 10 nembutal capsules were given per rectum; 7:00 p.m. patient unconscious and quiet; 10:35 p.m. patient restless, apparently having labor pains; 1:00 a.m. to 4:00 a.m. resting quietly; 7:15 a.m. patient still unconscious but restless at intervals of every two minutes, apparently having severe labor pains. Inspection showed perineum bulging; 7:50 a.m. patient delivered an apparently normal live infant. At 12 noon patient still unconscious; 1:15 p.m. patient restless; 2:15 p.m. 4 nembutal capsules were given per os; 3:00 p.m. patient resting quietly; 8:00 p.m. patient semiconscious. From 12:00 p.m. to 6:00 a.m. patient slept with slight restlessness and at 6:00 a.m. condition improved, talking; 9:30 a.m. patient much improved, cooperative, and asked for water and food when wanted. No further complaints. There was a gradual fall in the blood pressure to 122/84. The mother with her baby was discharged as cured on the twelfth day postpartum. There were no more convulsions after the first use of nembutal. It must be understood that in all our cases other active measures for combating the toxemia were included.

The results of our observations and experience warrant the following definite conclusions:

- 1. That nembutal eminently fulfills the described need for a drug capable of preventing convulsions but free of any possible harmful effect on organs already damaged.
- 2. That early treatment of preeclampsia including the use of nembutal precludes the occurrence of eclampsia.
- 3. That nembutal prevents, promptly stops, and effectively controls convulsions in the treatment of preeclampsia and eclampsia.

The problem of preeclampsia and eclampsia is a problem of toxemia and convulsion, potential or actual. Nembutal effectively controls the latter and with this control the former is clinically mitigated. Its specific rôle is not clear and further investigations are aimed at an explanation of this mechanism.

FATALITIES

There were three deaths in our series. The first occurred in a patient brought into the hospital comatose and with a temperature of 104° F.; death followed closely the second intravenous injection of magnesium sulphate 10 per cent, 20 c.c. each. As this case was an emergency, time did not permit a determination of the concentrating ability of the kidneys, which, if low, would have contraindicated the use of the magnesium sulphate. Hirschfelder and Serles¹ state that "coma simulating that of uremia may result from magnesium sulphate in patients with badly diseased renal tubules"; whereas, Murphy and Koppanyi,² Pratt³ and Gillespie⁴ have demonstrated experimentally that nembutal does not impose an extra burden on the kidneys. The second death occurred in a patient given morphine sulphate before entering the hospital and generous doses of chloral hydrate per rectum after admission.

It is regretted that a necropsy was not obtainable in either of these cases.

SUMMARY

- 1. In thirty-five treated cases of preeclampsia, nembutal prevented the onset of convulsions; whereas, three patients treated without nembutal developed convulsions.
- 2. Nembutal promptly stopped and completely controlled the convulsions in twenty-four treated cases of eclampsia.
- 3. The use of nembutal, per os, intravenously, or per rectum, in the treatment of preeclampsia and eclampsia is clinically superior to, and safer than, chloroform, morphine, chloral hydrate, or magnesium sulphate in the prevention and control of convulsions.
- 4. With the control of convulsions, clinically, the toxemia subsides. The rôle of nembutal in this complex is now under investigation.

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CYSTITIS EMPHYSEMATOSA

REPORT OF CASE

RAYMOND S. ROSEDALE, M.D., M.S. (MED.), BUFFALO, N. Y.

(From the Department of Pathology, Buffalo City Hospital and the University of Buffalo Medical School)

THE pathology and literature concerning cystitis emphysematosa has been well reviewed by Mills, 1, 2, 3, 4, 5 Hueper, 6 Putschar, 7 and recently Sanes and Doroshow, 8 so that our purpose in this communication is to report only the essentials of one additional case; not more than thirty cases have been described previously.

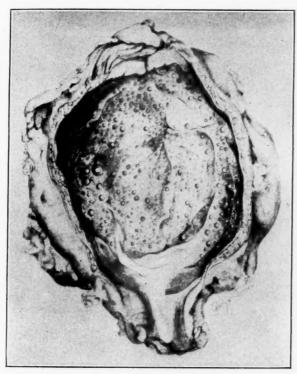


Fig. 1.—Drawing of the dissected bladder. Note the size, form, and distribution of the gas vesicles.

K. F., a white female, sixty-eight years of age, was admitted to the Buffalo City Hospital Oct. 5, 1934, complaining of pain in the lower abdomen, nausea, and vomiting, lasting one week.

The pupils were irregular, unequal, and did not react to light. There was congestion in both lung bases. A precordial systolic murmur and an aortic diastolic murmur were present. The blood pressure was recorded as 200/40. The abdomen was slightly distended, tender, and tense. The interphalangeal joints were enlarged.

There were 20.3 mg. of urea, and 131 mg. of glucose in 100 c.c. of blood. The blood glucose was recorded as 83 mg. per 100 c.c. in 1930. Ten per cent phenolsulphonephthalein was recovered the first hour. Urinalysis of October 8 was negative. The red blood cells numbered 3,650,000, and the leucocytes 10,800, 89 per cent were polymorphonuclear leucocytes and 29 per cent stabs. The temperature, pulse, and respirations varied from 98° to 103° F., 70 to 100, and 20 to 48 per minute, respectively.

A hypodermoclysis of 1,000 c.c. of normal saline was administered October 6, and at 10 A.M. October 9 she received 250 c.c. of 20 per cent glucose in normal saline intravenously.



Fig. 2.—X-ray of the dissected bladder. The dark shadows are due to the gas vesicles. The symbol I indicates the opened urethra.

Dysuria and incontinence were complained of on October 8, and 250 c.c. of dark-colored urine was obtained by catheter. The patient became moribund and death occurred October 9, at 2:40 P.M.

Autopsy.—The autopsy was performed two and one-half hours after death. The principal pathologicoanatomic findings were: gangrenous appendicitis, peritonitis, subdiaphragmatic abscess, degeneration of the parenchymatous organs, pulmonary congestion, and edema; chronic cholecystitis, diverticulosis of jejunum and colon; cystitis emphysematosa.

Bladder.—The bladder capacity was about 500 c.c. It contained only several cubic centimeters of slightly turbid urine which escaped when it was opened. There were many thin-walled semitransparent cystic elevations scattered throughout the entire

mucosal surface except immediately around the ureteral orifices. These vesicles varied in size from pinpoint to some as large as 1 cm. in diameter. The crests of

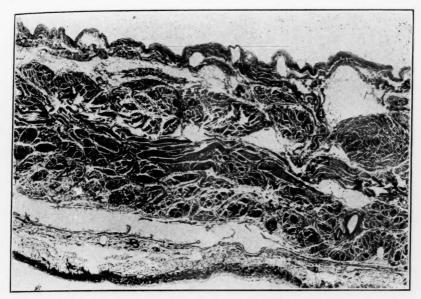


Fig. 3.—Photomicrograph 40×. Gas cysts are present in the lamina propria and upper portion of the muscularis. The serosa and subserosa are partly separated by artifact.

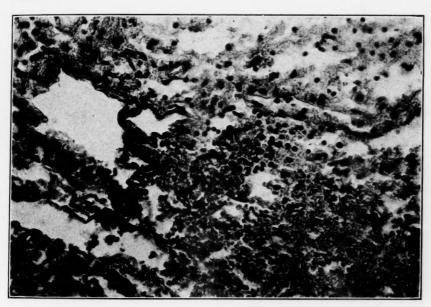


Fig. 4.—Photomicrograph 350×. Showing the hemorrhage in the interstitium.

some of the latter were elevated 4 mm. above the adjacent mucosa. In the left half of the bladder, particularly above the trigone, the mucosa was of a ruby red color, and within this field there were distinct small hemorrhagic areas.

The bladder wall measured 0.8 cm. in thickness. Palpation yielded a spongy crepitant sensation. Gas released from the vesicles by puncture was colorless, odorless, and noninflammable. The gas in some vesicles could be expressed into adjacent ones. A few gas vesicles were seen in the deeper layers of the bladder on its cut surface. The distribution, size and number of the vesicles are seen in Figs. 1 and 2. The gas from four of the cysts was withdrawn aseptically and replaced with sterile water which was then withdrawn and cultured aerobically and anaerobically. No organisms grew in these cultures within two weeks.

Postmortem cultures from the spleen were positive for *B. coli* and *B. welchii.* Streptococcus anhemolyticus developed in cultures from the abscess on the surface of the liver. Gram-positive cocci and bacilli were found in sections of the wall of the abscess.

Microscopic Examination.—In sections of the bladder the epithelium was desquamated entirely except in the deepest sulci. There was a diffuse infiltration of

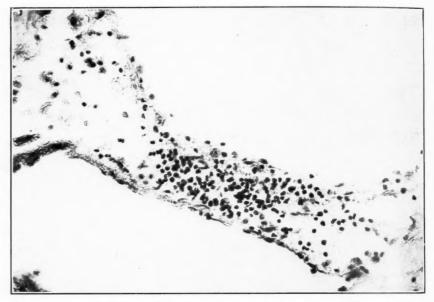


Fig. 5.—Photomicrograph 359 \times of a cyst wall. Note lymphocytes and an occasional polymorphonuclear leucocyte.

lymphocytes, a smaller number of plasma cells and an occasional polymorphonuclear leucocyte into the subepithelial lamina propria. In this there were also a few darkly staining multinucleated giant cells.

Cyst-like spaces were found principally in the lamina propria, but were also present in the muscular layers. Most were ovoid, with a smooth lining, but some were irregular in outline. The most superficial ones were roofed by thin fibrils of connective tissue. Their wall and lining was composed of collagen fibers and in the latter no endothelial cells were seen. A flattened spindle-shaped nucleus, apparently that of connective tissue, was found at the periphery of some of the gas vesicles. There were large collections of red blood cells free in the tissues, focal clusters of lymphocytes and a few plasma cells in relation to some of the cysts.

The entire thickness of the wall exhibited evidences of edema. Some of the larger veins were moderately filled with blood. An inflammatory exudate (from the peritonitis) consisting of fibrin, lymphocytes, and leucocytes, was present on the serosa. In this, large gram-positive bacilli with rounded ends, which morphologically

suggested B. welchii, and gram-positive cocci were found. No organisms were seen in the muscle layers or lamina propria in the same sections, or others stained by the same method.

COMMENT

The cystitis emphysematosa in this case, similar to some others previously reported, developed in the course of an infection elsewhere in the body. Also, as in some of the other cases, no organisms were recovered from the gas cysts.

On first thought one might consider the cystitis emphysematosa in our case to be due to septicemia. The absence of gas-producing organisms by stain and culture, in the cysts, their walls, lamina propria and muscle layers would indicate that this was not so. Likewise the absence of any foaminess of the liver and microscopically, the absence of gas vesicles in this and other organs would indicate that the emphysematous lesion was localized in the bladder and not part of a generalized disseminated gas producing infection. B. coli and B. welchii are common postmortem and terminal invaders in the spleen, especially in the presence of peritonitis from perforation of hollow viscera, and are so regarded here.

Causative microorganisms were not demonstrated in the cystitis emphysematosa in this case. It has been stated by J. A. McIntosh⁹ that if the gas from such cases is inflammable it has been developed by the action of *B. welchii*. The author has had no experience in this regard but wishes to point out that the gas in the vesicles in this case could not be ignited in several trials.

It has been stated usually that the vesicles were lined by endothelium, and the cysts have in some instances seen regarded as lymphatic channels containing gas. In this case it could not be satisfactorily demonstrated that any lymphatics were involved, and furthermore none of the regional lymph nodes exhibited evidences of emphysema.

In more than half the number of reported cases there has been diabetes, or glucose in saline has been administered by clysis. The individual in the case reported here received 50 gm. of glucose intravenously four hours and forty minutes before death. We feel, as first expressed by Hueper, and amplified by Sanes and Doroshow, that the increased glucose in the urine and bladder tissues may be an etiologic factor, and that here, as in other cases, notably that of R. G. Mills, the trauma of catheterization also may be considered.

Acknowledgment is made to Dr. W. F. Jacobs for his review of the material.

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Lefevre, H., and Blanc, H.: A Case of Acute Dilatation of the Ureter Following a Circumscribed Abscess in the Base of the Broad Ligament, Bordeaux Chirurgical 16: 129, 1935.

A case of acute dilatation of the left ureter, subsequent to an abscess in the broad ligament, is described. The authors, however, do not consider the dilatation due to mechanical blockage by the abscess, but that it was produced by ureteral paralysis from the toxemia of the abscess. They believe their contention is supported by the lumbar region pain and renal hypersensitiveness before operation.

J. THORNWELL WITHERSPOON.

OBSERVATIONS ON CONCENTRATION OF ANTERIOR PITUITARY-LIKE HORMONE IN THE URINE IN CHORIONEPITHELIOMA, WITH REPORT OF A CASE

JOSEPH M. LINETT, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics and Gynecology, Kings County Hospital)

I'N 1929 Robert Meyer and his assistant Roessler¹ were the first to observe the positive Aschheim-Zondek reaction from the urine of a terminal case of chorion-epithelioma. Since then about forty-five cases² of chorion-epithelioma have been reported in the literature in which the diagnostic and prognostic value of the test has been demonstrated.

Ehrhardt³ demonstrated 100 mouse units and Robert Meyer 70 mouse units of the anterior pituitary per cubic centimeter of urine in a case of chorionepithelioma. According to Mazer and Edeiken,⁴ the urine of a normally pregnant woman yields about 5 M.U. per c.c. Zondek describes studies in cases of hydatidiform mole, the concentration of the anterior pituitary hormone in the urine of these cases being two to three times greater than in normal pregnancy. Mack and Catherwood⁵ report positive reactions obtained in dilutions 1:10 in chorionepithelioma and in a dilution of 1:5 in a case of mole. Excessive concentration of the hormone in the urine, or a reappearance of it after a negative test had been obtained is strongly suggestive of chorionepithelioma.

The following case will illustrate this assumption and supplement those already cited in the literature.

Mrs. F. S., aged thirty-five years. First admission to Kings County Hospital, June 12, 1933. Chief complaint, vaginal bleeding. Last regular menstrual period occurred Dec. 22, 1932. Patient has had slight vaginal bleeding since March. About fifteen days prior to her admission to the hospital, patient had a severe hemorrhage; she was placed abed. Since then vaginal bleeding was slight. Just before admission patient began to bleed excessively. There was no pain or toxic symptoms.

The family and her past history were irrelevant. Menses began at fourteen years of age, twenty-eight-day type, flow moderate, lasting from three to four days. Patient has three normal children, no previous miscarriages.

Physical Examination.—An obese Italian woman. Head, neck, heart, and lungs normal. On abdominal examination the height of the fundus was suggestive of a six-months' pregnancy. On vaginal examination the cervix was two fingers dilated. Few clots and cysts were found in the vagina. Blood pressure 110/78; R.B.C. 4,064,000; hemoglobin 80 per cent; morphology normal; W.B.C. 9,400; polymorphonuclear 67, small mononuclear 31, large mononuclear 2. Urine negative. A diagnosis of hydatidiform mole was made. On the day of admission patient had severe cramplike pains in the abdomen and passed, by vagina, a large mole. On the following day she was transferred to the gynecologic service. On June 18 the Friedman test was reported negative. On the following day a dilatation and curettage was done. The depth of the uterus was about 9 cm. A small amount of tissue was removed.

The pathologic report is as follows: The section consisted of blood clot and degenerated decidual tissue; also a portion of endometrium showing the glandular hypertrophy usually observed in cases of pregnancy. No evidence of hydatid mole. Diagnosis: Endometrium of pregnancy.

Postoperative course was uneventful, the patient was discharged June 21, 1933, nine days after admission to the hospital, and advised to report to the gynecologic clinic.

On Nov. 18, 1933 the patient was readmitted. Her menses were normal in July, August, and September. The September period was one week overdue. Since that time patient has had slight amount of vaginal bleeding which would disappear when abed only to reappear when walking. Two days prior to her admission she began to bleed profusely. She then presented herself at the Kings County Gynecologic Clinic where she was advised to enter the hospital. Physical examination showed an obese woman markedly anemic. Lungs negative. Heart sounds rapid with a soft systolic at the apex.



Fig. 1.—Uterine curettings June 19, 1933, degenerated decidual tissue and glandular hypertrophy.

Vaginal Examination.—Marked bleeding from vagina. Cervix soft, admits one finger. Uterus and adnexa not palpated because of obesity of abdominal wall. Blood pressure 120/60. Patient was sponge-sticked and a large amount of placental tissue was removed. Following the emptying of the uterus vaginal bleeding ceased. Temperature normal, pulse 96. Patient was discharged Nov. 22, 1933 with a diagnosis of incomplete abortion.

On Nov. 27, 1933 the patient was received from the Harbor Hospital ambulance bleeding profusely from the vagina. She appeared markedly anemic with an anxious expression. Temperature 104, pulse 124, and respiration 26. Vaginal examination revealed a bluish tumor on the posterior surface of the vaginal wall just below the cervix, size of a hen's egg. A piece was removed accidentally and sent to the laboratory. Cervix soft, admitted one finger, bled moderately. Uterus irregular, enlarged to the size of two-months' pregnancy. Small piece of placenta-like tissue removed from the uterus and sent to the laboratory.

Pathologic report by Dr. Hala. Tissue from uterus. Small pieces of blood clot. Microscopic: The section consisted of blood clot and portion of a tumor, composed largely of Langhans' cells with only occasional syncytial elements present. The

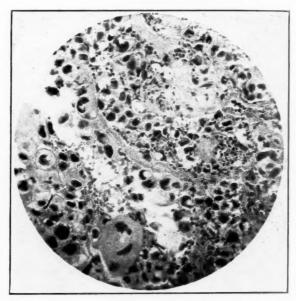


Fig. 2.—Tissue from uterus, atypical proliferation of Langhans' cells and syncytial elements.

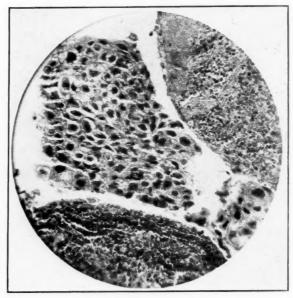


Fig. 3.—Tissue from tumor mass of posterior vaginal wall. Masses of Langhans' cells of varying size.

alveolar arrangement, the hypertrophy of the cells, and the presence of occasional mitotic figures would suggest that this was a chorionepithelioma.

Tissue from tumor of posterior vaginal wall. Microscopic: The section consisted of organized blood clot within which were noted masses of Langhans' cells of varying size. These cells were palisaded or in alveolar formation. Hypertropic types and occasional mitotic figures suggest chorionepithelioma.

On the day of admission the patient had a free hemorrhage which necessitated packing. Hemoglobin 40 per cent; R.B.C. 2,176,000; W.B.C. 6,800; polymorphonuclear 61; lymphocytes 30. Blood pressure 90/60. Sedimentation time seventy minutes. Blood chemistry, Wassermann, and urine negative. On the day after admission patient was given 500 c.c. of blood by transfusion. On December 9, R.B.C. 1,504,000, and hemoglobin 28 per cent. Patient received two more transfusions during her stay in the hospital. Roentgen ray studies of the lungs were negative for metastasis. The patient was subjected to two intensive x-ray treatments of the pelvis.

Six rabbits were injected with patient's urine in the following dilutions:

- 1. Injected with urine in dilution 1:20 Both ovaries show multiple hemorrhagic cysts
- 2. Injected with urine in dilution 1:40 Same
- 3. Injected with urine in dilution 1:80 Same
- 4. Injected with urine in dilution 1:160 One ovary shows one hemorrhagic cyst
- 5. Injected with urine in dilution 1:320 Same
- 6. Injected with urine in dilution 1:600 No hemorrhagic cysts observed

The toxic condition of the patient and the anemia gradually increased until her death on Jan. 10, 1934, six weeks after her third admission to the hospital. No postmortem was obtained.

COMMENT

- 1. The anterior pituitary hormone reappeared in the urine after a negative test had been obtained.
- 2. A quantitative relationship between the concentration of the hormone in the urine and the proliferation of the tumor mass is shown.
- 3. Had this case been studied by the Aschheim-Zondek test, following the expulsion of the mole, proper therapeutic measures instituted early might have checked the progress of the condition.

I wish to thank Mr. Yonke for carrying out the Friedman Test and Drs. Duncan and Rynd on whose services the case occurred.

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Repetti, M.: The Vitamin A Content of Human Colostrum, Folia gynaec.demograph. 31: 337, 1934.

The author's experimental studies establish the fact that the vitamin A content of colostrum is five times that of human milk. He concludes, because of that fact, it is important that the newborn be placed to the breast in the colostrum-excreting stage of lactation and makes a plea for a diet rich in vitamins during pregnancy and lactation.

THE EFFECT OF SYMPATHETIC DENERVATION UPON OVULATION AND ESTRUS IN THE RAT*

HENRY G. SCHWARTZ, M.D., AND C. LEE BUXTON, M.D., BOSTON, MASS. (From the Department of Anatomy, Harvard Medical School)

IN 1929 Cannon and others² found that one female cat conceived when the splanchnic nerves were the only remaining sympathetic fibers; six weeks after extirpation of the splanchnics, normal parturition occurred. Further experiments performed in his laboratory^{1,5} showed that removal of the abdominal sympathetic trunks had no

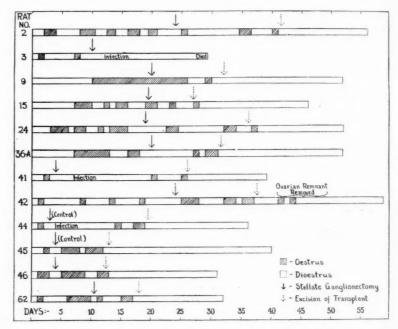


Fig. 1.—Graphic representation of course of estrus and diestrus following oophorectomy and transplantation of ovaries into the antecubital fossa.

noteworthy effect upon the recurrence of the estrous cycle in white rats. These observations were confirmed by Herren and Haterius,³ and nicotinization was reported by Thienes⁶ to have no effect upon ovulation. It was previously found,⁴ in oophorectomized female rats bearing ovarian transplants (in the spleen, mesometrium, and anterior abdominal wall), that estrous cycles occurred soon enough after transplantation, to rule out the establishment of new reflex arcs.

In the present work the authors have attempted to study the problem of neurologic influence upon the estrous cycle by a direct method

^{*}This investigation was financed in part through the generosity of E. S. Wilkinson.

which would rule out two major objections, namely, (1) the possibility of failure to remove all of the finer ramifications of the abdominal sympathetic chain in the rat; and (2) the possibility of new nervous connections accompanying the blood vessels.

Eighteen female white rats were used. After regular cycles were found to be present, by means of daily vaginal smear examination according to the criteria of Long and Evans,⁴ both ovaries were removed and transplanted into the antecubital

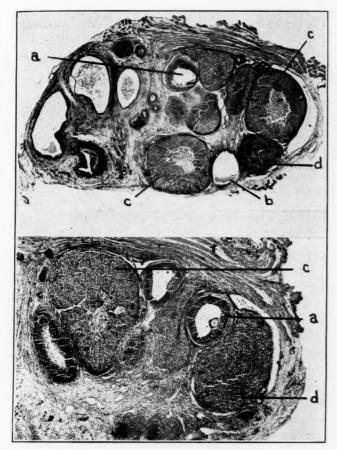


Fig. 2.—Photomicrographs of sections of ovaries transplanted into the antecubital fossa. (For description, see text.)

fossa of the right forelimb. Subsequent vaginal smear examination showed "takes" in all of the animals. Following the establishment of estrous cycles, sixteen rats were subjected to excision of the stellate ganglion on the right side. Previous dissection of normal rats showed that this procedure would effectually deprive the right forelimb of all sympathetic innervation. The operation was performed extrapleurally, through a posterior incision into the first intercostal space. The ganglion was excised, under direct observation through a binocular loupe. The method entailed a certain degree of risk, especially at first, due chiefly to the tenuousness of the pleural membrane in the rat. Of the 16 animals, 10 rats sur-

vived the operation. As controls, 2 of the original 18 were subjected to the same operative procedure, omitting only the excision of the ganglion.

The results are represented in Fig. 1. In all cases except one (Case 3), the estrous cycle recurred following sympathetic denervation. The excepted animal suffered from a pyogenic infection of the posterior thoracic incision, resulting in lung abscess, inanition and death. This course may account for the absence of cycles. Vaginal smears showed signs of estrus in seven animals within five days after removal of the stellate ganglion; in one (No. 36A) estrus did not occur until the eighth postoperative day; and there was a delay of seventeen days in No. 41. One of the controls (No. 45) went into estrus shortly after the control operation, while the other (No. 44) delayed for twelve days. The tardy appearance of estrus in Nos. 41 and 44 may have been due to slight infection. Following the reappearance of estrus the cycles appeared to be normal, so that we cannot claim any effect of sympathetic denervation.

When the recurrence of normal cycles was established, the ovarian transplants were removed. Subsequently, except for several expected instances of immediate postoperative estrus, cycles were abolished in all the animals except No. 42; in this case it was found that not all of the transplant had been removed. Following extirpation of the small remaining fragment, the cycles abruptly ceased. These results confirm the physiologic activity of the transplants. For a further check, serial sections were made of the excised ovarian tissue. In Fig. 2 are photomicrographs showing the presence of ripe follicles (a), freshly ruptured follicles, (b), mature corpora lutea (c) and old corpora lutea (d).

Direct proof of the absence of sympathetic innervation to the arm was obtained after the ganglionectomized animals were killed and necropsied. Under a binocular loupe the right sympathetic chain was dissected from above and below to the site of the operation (stellate ganglion). Grossly, no new sympathetic connections had been made. Histologic study of the scar revealed no sympathetic ganglion cells. Examination of the control rats showed normal stellate ganglia.

CONCLUSIONS

- 1. A method is presented by which all sympathetic innervation is excluded from transplanted tissue.
- 2. By the use of this method it is demonstrated that the presence of the sympathetic nervous system is not essential in ovulation and the production of estrus.
- 3. Ovaries transplanted into the antecubital fossa are shown to be active by physiologic and anatomic criteria.

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MULTIPLE ARRHENOBLASTOMA OF THE OVARY

A. M. GNASSI, M.D., JERSEY CITY, N. J.

(From the Pathological Department, Jersey City Medical Center)

 $T_{\rm rarity}$ of the tumor, and because, in a search of the literature, it is the only case of multiple arrhenoblastoma that I have been able to find.

Mrs. A. R., forty-three years old, white waitress, was admitted to the hospital complaining of pain in the lower right quadrant of the abdomen of seven weeks' duration. Her general health had been good except for an attack of appendicitis for which she was operated upon in 1927. Her menstrual periods started at twelve, regular, twenty-eight days, and lasted seven days. She was married in June, 1915, and had had normal marital relationships. Two months following her marriage, at the age of twenty-four, her menstrual periods suddenly ceased. In September, 1915, she consulted a physician who told her she was pregnant. The pregnancy, however, never materialized. During 1918 and 1919, she had several attacks of laryngitis and noticed that her voice gradually became huskier. Treatment for this was of no avail. At the end of 1919, she noticed a scanty growth of soft, silky hair on her face, chest, abdominal wall, and legs which became more noticeable as time passed. She treated this with depilatories and bleaches, but later she was forced to shave. During the last four years, she was compelled to shave every day.

The onset of the present illness dated seven weeks before admission with pain in the lower right quadrant which she described as "hanging and pressing and radiating to the back." This pain became increasingly severe, and a week before admission, she had to give up work because of its severity and because of the onset of vomiting. The only significant fact in the family history was that her mother died at the age of thirty-eight after an operation for a tumor, the nature of which is not known.

Physical examination revealed a masculine type of middle-aged woman, weighing 130 pounds and measuring 5 feet, 6 inches in height, lying comfortably in bed and not acutely ill. Her scalp was covered with thick, black, coarse, bobbed hair. There was a conspicuous male distribution of hair on face, neck, axillae, abdominal wall, and pubis, and the eyebrows were bushy. The voice was husky and deep, and the skin rough, thick, and dry. The breasts were small and flat, the nipples coarse and rather heavily pigmented, and the areoli studded with thick, long, dark hair. The heart and lungs were normal. The abdomen revealed no masses. The pelvis was small and masculine in type. The clitoris was hypertrophied, the prepuce prominent, the cervix small, the introitus narrow, and the uterus small with a second degree retroversion. There was a small, tender mass in the right fornix. The temperature was normal and the blood pressure was 135/80.

The report from the clinical laboratory was as follows: red blood cells 4,240,000 per c.mm.; hemoglobin 80 per cent; white blood cells 8,200 per c.mm.; differential cell count, 75 per cent polymorphonuclear neutrophiles, 22 per cent lymphocytes, 3 per cent large monocytes; Wassermann negative; urinalysis, acid, specific gravity 1.015, traces of albumin, few leucocytes.

The preoperative diagnosis was cyst of the ovary; prolapse of uterus. Operation was performed Sept. 25, 1934, under spinal anesthesia. A low median line incision was made. The right ovary was smooth but lobulated, the round ligament relaxed,

with secondary prolapse of the uterus. A right cophorectomy and plication of the round ligament was done. The patient had an uneventful recovery and was discharged from the hospital ten days later.

On Jan. 23, 1935, at the age of forty-one, the menses recurred after an amenorrhea of twenty years. It lasted two days and has recurred regularly at four-week intervals to the present time. The hair is soft now, but no other changes have been noted to the present time.

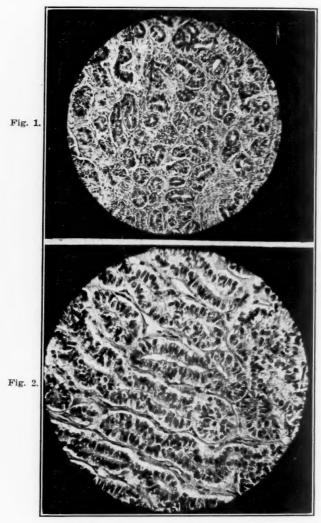


Fig. 1.—Low-power magnification of a typical field showing convoluted, elongated or round tubules.

Fig. 2.—High dry magnification showing elongated tubules and scanty and partially hyalinized stroma.

PATHOLOGIC REPORT

Gross Description.—The specimen, received in 10 per cent formalin, was an ovary which measured 6.6 cm. by 4 cm. by 2.8 cm. The surfaces were smooth, gray, and somewhat lobulated. On section through the long axis, four chrome yellow bodies

were seen. They were well demarcated and easily shelled out. The first was round and measured 0.9 cm. by 0.9 cm. by 0.8 cm. The second, elliptical, 0.7 cm. by 0.6 cm. by 0.5 cm.; the third, oval, 0.9 cm. by 0.8 cm. by 0.1 cm., and the fourth, 0.7 cm. by 0.6 cm. by 0.5 cm.

The cut surfaces of the bodies were yellow and finely granular. The supporting tissue was firm and gray and conspicuous for the absence of corpora lutea and follicular cysts.

Microscopic Description.—The four tumors had the same histologic structure and therefore will be described together.

The tissue was stained by three different methods: with hematoxylin-eosin, with Sudan III, and with Mallory's triple stain, after washing in water and refixed with Zenker's solution.



Fig. 3.—Oil immersion magnification showing closely related glandular structures resembling seminiferous tubules,

Sections showed closely related groups of convoluted, elongated, and round tubular acini lined with cuboidal or roughly spheroidal or columnar cells which had acidophilic nuclei. The nucleoli were inconspicuous, but when found were large and pale. Vacuolization of the cytoplasm, and to a lesser extent, of the nuclei was observed. The basement membrane was ill defined or absent. In places, the epithelium proliferated to partially or completely obliterate the lumen, in the latter case, leading to the formation of irregular groups or nests of cells which occasionally showed marked degenerative changes with some inflammation. In a few places, the epithelium was arranged to resemble closely the medullary cords of the gonads. In other places, there were areas of closely packed spindle-shaped cells which had hyperchromatic nuclei and occasional mitotic figures. In this region, the blood supply was scanty and the blood vessels well formed. The remaining portions of the tumor were moderately vascular. The inter- and intraluminal blood capillaries were

congested and well formed. The supporting stroma was scanty and markedly hyalinized. Within the supporting tissue of the acini, there were single or nests of polyhedral cells which had finely granular, slightly acidophilic cytoplasm and spheroidal and prominent nuclei, containing coarse, darkly stained chromatin granules and one or occasionally two large, heavily stained nucleoli. These cells did not display any particular relation to the blood vessels and morphologically were identical with the interstitial cells seen in the testis.

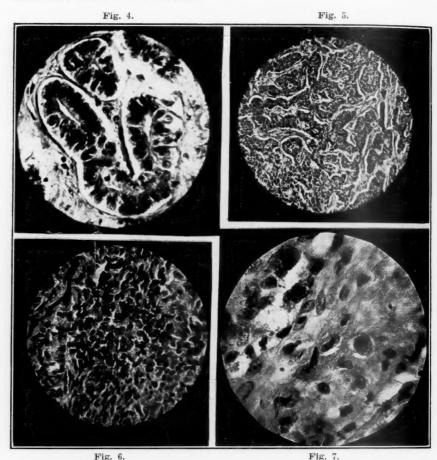


Fig. 4.—Oil immersion magnification showing the epithelium to be limited by a definite membrana propria.

Fig. 5.—Low-power magnification showing cords resembling the medullary cords of the undifferentiated gonad.

Fig. 6.—High dry magnification of a field showing sarcoma-like structure.

Fig. 7.—Oil immersion magnification of a field showing interstitial cells resembling those of the testis

Sudan III showed the epithelial and interstitial cells to contain a moderate number of fat globules. Polarized light showed double refracting crystals to be conspicuous in the interstitial cells. The epithelium occasionally reacted positively to this test.

This case illustrates the powerful influence of the hormones produced by the tumor in exerting its defeminizing and masculinizing effects. It is still more remarkable that after the tumor was removed, the menstrual cycle reappeared after almost twenty years' suppression.

I wish to thank Dr. J. M. Rector for allowing me to abstract the case and Dr. A. V. St. George for his valuable advice.

ON THE ORIGIN OF THE AMNIOTIC FLUID

WITH EXPERIMENTAL AND CLINICAL OBSERVATIONS H. ACOSTA-SISON, M.D., MANILA, P.I.

(From the Department of Obstetrics, University of the Philippines)

THE origin of the amniotic fluid is still an object of speculation. Williams¹ mentions four theories, namely: (1) The amniotic fluid is a transudate from the blood serum, (2) it is a collection of fetal urine, (3) it is a secretion from the amnion cells, or (4) it has a mixed origin.

Zangemeister and Meissl,² Makepeace, Freemont, Smith, Dailey and Carroll;³ and Cantarow, Stuckert and Davis⁴ are of the opinion that while the amniotic fluid may primarily originate from the blood serum, it is increasingly admixed with fetal urine as the age of pregnancy advances.

Zangemeister and Meissl² reached their conclusion by noting the difference in the freezing points of the maternal blood serum and amniotic fluid, the latter being always hypotonic from the fifth month of pregnancy onward. They found that the hypotonicity of the amniotic fluid increases toward term. They found too that the fetal urine is markedly hypotonic, and they attributed the hypotonicity of the amniotic fluid to its increasing dilution with the fetal urine. In the earlier months, the hypotonicity of the amniotic fluid is much less as confirmed by Gruenbaum.⁵

Makepeace³ and his associates based their opinion on the data obtained from a comparative study of the chemical composition of 33 simultaneous samples of human blood serum and amniotic fluid. They found that the amniotic fluid has greater concentration of creatinine or creatinine-like substances, more protein, less sodium, and slightly more sodium chloride than the maternal serum. They agree with Zangemeister and Meissl² that the amniotic fluid is hypotonic and that in the earliest months, it may be isotonic with the maternal serum. They state that the amniotic fluid approaches the composition of other protein poor fluids which are in osmotic equilibrium with the blood plasma.

Cantarow4 and his coworkers believe the amniotic fluid cannot be a pure dialysate of maternal blood plasma. Their belief is based on the comparative study they made on human amniotic fluid and maternal blood serum obtained at the seventh to the ninth month of pregnancy and on the comparison made between the amniotic fluid and other body fluids. They determined in both the amniotic fluid and maternal blood serum, the protein, nonprotein nitrogen, uric acid, sugar, calcium, and phosphorus concentrations. They failed to find any correlation between the amniotic fluid and the blood serum. They found the amniotic fluid to have less protein, more nonprotein nitrogen, much higher uric acid, less sugar, less calcium, and slightly more inorganic phosphorus. And, after comparing the chemical composition of the amniotic fluid with the cerebrospinal fluid, the peritoneal, and pleural transudates, they believe that the values obtained for the amniotic fluid would justify the theory of its being a dialysate or transudate if it were not for its high uric acid content.

Stroganoff⁶ attributes the benefit derived from early rupture of membranes in eclampsia to be due to the reduction of absorption of liquor amnii with its extractive substances (supposedly derived from fetal urine) and ferments into the maternal circulation,

Schmidt⁷ believes that on the basis of histologic studies of the amnion, the amniotic fluid is a secretion of the placental amniotic epithelium. Polano and Williamsi independently describe vacuoles and fat droplets in some amniotic cells which they believe to be an indication of secretory activity.

As confirmatory of the above theories, I wish to present the following experimental and clinical observations.

The experiments were primarily conducted to find the routes by which substances in the maternal circulation could reach the amniotic fluid and also to find how readily substances in the maternal circulation could reach the fetus.

Experiment 1.—A pregnant guinea pig was injected intracardially with 13 c.c. of methylene blue solution (2.1 per cent). It aborted twelve hours afterward two almost full-term fetuses which on autopsy showed no blue stain whatever. The mother guinea pig survived the experiment and eliminated the dye through the urine.

Experiment 2.—Experiment 1 was repeated with another pregnant guinea pig but with a very concentrated solution (2.1 per cent) of methylene blue. After the injection of 5 c.c. the skin of the extremities, eyelids, and secretion from the genitalia became bluish. On opening the abdomen, the abdominal muscles and peritoneum were not stained. The liver, intestines, kidneys, and bladder were deeply stained. The spleen was stained only in parts but not uniformly. Only the lower part of the uterus near the vagina was stained. The upper part of the uterus, the placenta, the amniotic fluid, and fetuses were free from stain. The heart and neck glands were deeply stained, but not the lungs or brain. The diaphragm was well stained but not the skeletal muscles.

Experiment 3.—Fifteen cubic centimeters of strong carbolfuchsin solution (1 per cent) was injected intracardially into a pregnant guinea pig. The skin and all the abdominal organs, especially the intestines, were well stained. The bladder and the uterus were well stained but not the urine. The reason for this is perhaps that the urine was already there before the injection was made. The heart, liver, lungs, and kidneys were well stained. The skeletal muscles were not as well stained as the organs. The placentas (three) and the placental end of the cords were stained but not the amniotic membranes, amniotic fluid, nor fetuses.

Experiment 4.—Under chloroform anesthesia, methylene blue solution was injected into the uterine artery of a pregnant guinea pig. The uterus and placenta, especially the former, were stained. The organs of the fetus were only slightly stained but not the skin nor amniotic membrane nor amniotic fluid.

Experiment 5.—Carbolfuchsin solution was injected into the placenta. Result: The membranes, patches of the skin of the fetus, and part of the fetal intestines became stained but the amniotic fluid remained clear.

Experiment 6.—Methylene blue was injected into the umbilical vein and immediately the skin of the fetus and its organs became deeply stained.

Experiment 7.—Thirty cubic centimeters of methylene blue (2.1 per cent) was injected into the abdominal acrta of a pregnant cat. The placentas, membranes, and the placental³ end of the umbilical cords of the fetuses became stained. The amniotic fluid was only slightly stained. The skin of the fetuses was stained in patches, in those regions in direct contact with the membranes. The fetal organs including the kidneys were not stained.

Experiment 8.—Under chloroform anesthesia, a pregnant cat was injected with methylene blue into the uterine artery and also into the space between the amnion

and placenta. The membranes became stained in a small patch at first, but the staining of the membranes spread rapidly into the rest of the membranes, placenta, and umbilical cord. The amniotic fluid became slightly stained. The skin of the fetus became stained in patches in those portions that came in direct contact with the membranes. The internal organs of the fetus were also stained.

CLINICAL OBSERVATIONS

Observation 1.—A case of dystocia due to fetal bladder distention caused by retention of urine as a result of absent urethra.

The patient was brought to the hospital from a near-by province with badly damaged lower extremities of a seven months' fetus dangling from the introitus. It was soon found that the cause of the unsuccessful extraction of the fetus was its enlarged abdomen. It was punctured and about 500 c.c. of clear fluid gushed out.

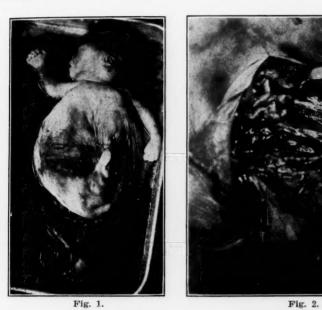


Fig. 1.—Fetus with hydroperitoneum and dilated bladder due to absent urethra.

Fig. 2.—The dilated bladder showing the blind ending of the sigmoid colon on its wall.

The extraction of a male fetus could thereafter be made but with some difficulty due to the still distended abdomen. Five minutes afterward an alive female child was born spontaneously, followed ten minutes afterward by the expulsion of two placentas which apparently were normal.

Examination of the stillborn baby revealed it to be a small fetus with an enormously distended abdomen. The umbilicus which occupied a circle with a diameter of 7 cm. was 21 cm. above the symphysis pubis. The peritoneal cavity was intact containing about 500 c.c. of clear fluid. It was found that what was punctured was the enormously distended bladder whose wall attachments occupied the whole pelvic cavity and lower abdominal wall. There was no urethra, no rectum, and no anus. The sigmoid ended in an attenuated blind solid cord in the left wall of the bladder (Fig. 2). The kidneys were lobulated and quadrangular in form.

The history of this patient showed that very scanty amniotic fluid was associated with the first baby.

Observation 2.—Pressing the bladder region of a five months' fetus miscarried by A. R. on Aug. 20, 1929, elicited the passage of a few drops of urine.

Zangemeister and Meissl² also mention having been able to express urine from a five months' miscarried fetus.

COMMENT

The results obtained from Experiments 1, 2, 3, 4, and 5 on guinea pigs show that because of the small caliber of the blood vessels, the stain does not readily pass through the placenta into the fetus or to the amniotic fluid.

Experiment 6 shows the ready staining of the fetus when the placenta and membranes do not constitute a barrier. The result of Experiments 7 and 8 where the larger blood vessels of the cat have been used, shows that the dye passes from the maternal circulation into the fetus through the placenta and into the amniotic fluid through the placenta and the amniotic membrane. Apparently, it shows the amniotic fluid to come from the maternal circulation through the intervention of the amniotic membrane. Since the amniotic membrane in relation to the placenta comes in contact with blood vessels larger than those in contact with the atrophied decidua capsularis, it is presumed that most of the fluid from the maternal circulation comes from that portion in immediate contact with the placenta.

The result obtained from the above experiment and the cited clinical observations fit in with the chemical examination of the amniotic fluid made by the above cited investigators who state that though the amniotic fluid may originally come from the placental circulation through the intermediation of the amnion, it must be increasingly admixed with fetal urine after the full development of the kidneys.

Clinical observations showing either scanty amniotic fluid or the retention of urine due to absent urethra, and the unmistakable proof that fetal urine is excreted as early as the fifth month if not earlier, conclusively prove that though the amniotic fluid may originally come from the placental circulation through the intermediation of the amnion, it must be increasingly admixed with fetal urine after the full development of the kidneys.

The increase of the amniotic fluid as the age of pregnancy advances after the fourth month is due not only to the larger circulation in the placenta but also to the added amount of fetal urine which is excreted into it.

That the amniotic fluid is not static but becomes changed through the maternal circulation is shown by the investigations of Albano⁸ who after injecting into the amnion 6 mm. of sodium-phenol sulphonaphthalate noticed its gradual disappearance until the end of fortyeight hours. He believes the liquor amnii is renewed every 14.31 hours.

CONCLUSIONS

The result obtained from Experiments 5, 7, and 8 in conjunction with the cited clinical observations as well as the result of the physical and chemical analysis of the amniotic fluid and the histologic examination of the amnion by independent groups of investigators justifies the conclusion that the amniotic fluid primarily originates from the placental circulation which may include that of the cord through the intervention of the amniotic epithelium, but that after the fifth month of pregnancy if not earlier, it is increasingly admixed with fetal urine.

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Of the 25 patients studied, 5 had acute and 20 had chronic syphilis; of the latter, some had but "serologic" syphilis, and others, discoverable macroscopic disturbances in one system or another. In not one of these, however, was a single semen study positive for Spirocheta pallida.

Spirocheta pallida is known to occur in the semen of a definite percentage of patients with untreated acute and chronic syphilis. This fact was generally ascertained by an examination of one specimen of semen and whereas in the present study Spirocheta pallida was conspicuous by its absence in all cases examined, a definite sterilizing effect of at least the neoarsphenamine and bismuth compounds upon the semen of patients with syphilis would appear to be a certainty. The value of this study lies not only in demonstrating the noninfectiousness of the semen of patients under treatment for syphilis but in indicating a method of testing syphilitic men who insist on marriage before they have had adequate therapy. It is a test of infectiousness that can be used before contemplated marriage in conjunction with the usual methods of examination,

C. O. MALAND.

Yagi, H., and Yamabe, A.: Hysterosalpingography in the New-born, Jap. J. Obst. & Gynec. 17: 412, 1934.

The authors injected iodized oil into the uteri of ten female, mature newborn babies (fresh specimens). They found that the uterine cavity and the fallopian tubes were permeable to the oil. They observed that the uterine cavity was small whereas the cervix was long. The fallopian tubes were indistinct and had many tortuosities. The pressure required to inject the contrast medium was between 200 and 250 mm. Hg. The authors conclude that hyperplasia of the uterus in an adult woman stands midway between the uterus of the newborn and the fully developed uterus of an adult woman.

J. P. GREENHILL.

VAGINAL HERNIA OF DOUGLAS' CULDESAC

R. J. STEARNS, M.D., OMAHA, NEB.

(From the Department of Gynecology, University of Nebraska College of Medicine)

THE literature dealing with true vaginal hernia of the posterior culdesac is not very abundant, even though it has been recognized and discussed for the past two hundred years by some twenty different men. In 1887, Etheridge reported on the subject, then nothing was written for about twenty-six years, when Lothrop gave quite an extensive review of the literature. Since that time a case has been reported every two to four years, the last ones by W. T. Black and J. H. Dew.

The terms used to describe this condition are many; such as, vaginal enterocele, posterior vaginal enterocele, culdesac hernia, Douglas pouch hernia, posterior vaginal hernia, high rectocele, hernia of Douglas, perineal hernia, vaginolabial hernia, and pelvic hernia. I think the most descriptive term is vaginal hernia of Douglas's culdesac, since it is a peritoneal sac pushed through an opening in the pelvic floor which presents as a bulging mass into some portion of the vagina.

Most textbooks on gynecology at least mention this condition, but with the exception of Kelly, they give no adequate description of it. The article in Kelly's *Gynecology* by G. G. Ward¹⁸ is very complete with some very good illustrations of the condition.

There are several types depending upon the point of exit through the pelvic floor. These points of exit may be anterior, as between the bladder and the uterus, lateral to the uterus, or the most common, posterior, as between the rectum and the posterior wall of the vagina.

The cause is probably a congenital weakness of the pelvic floor at this point associated with the strain of pregnancy and labor. The large majority of the cases cited in the literature have had one or more confinements. The conditions most often confused with this type of hernia are rectocele, cystocele, and uterine prolapse.

It is not always easy to diagnose these hernias as there may be no other symptoms than those associated with pelvic relaxation with the protrusion of either vaginal wall. At times the protrusion may change with respiration and entirely disappear upon reclining, the sac may contain coils of intestine in which the peristalsis may be elicited. The diagnosis is usually made not from any marked symptoms on the part of the patient that are due directly to this hernia; but in the course of an examination for some associated condition, such as uterine prolapse or a rectocele, this unusual bulging of the vagina is found. In some instances it is discovered following a perineal repair with a return of the apparent prolapse of the posterior vaginal wall or rectum, and on close examination it is found that the recurrent herniation is high up on the posterior vaginal wall.

The cure of this condition is, of course, a surgical one. There are several methods of operative procedure: Vaginal, abdominal, and the combined vaginal and abdominal method of approach. In the two cases I wish to report the patients were both operated upon by the vaginal route.

Case 1.—Mrs. W., University Hospital No. 49583, aged fifty-one, gravida iii, fifteen years ago the last child was born, all quite normal labors. She went through the menopause at forty-eight.

In her past history the only significant factor was a cardiac decompensation, now well compensated, but with fibrillating heart and a mitral stenosis. A marked ascites was present, which may have been a contributing factor by increasing the pelvic pressure.

Her immediate complaint was a discomfort when sitting or walking due to a constant protrusion of a mass from her vagina. This had been gradually getting worse since she first noticed it some eighteen months before entering the hospital.

She had been examined previously by three physicians, one making a diagnosis of rectocele the other two of prolapse of uterus. Examination in the prone position showed no evident protrusion from the vagina but after much effort at straining there was extruded the cervix and posterior vaginal wall. Fig. 1, which is an actual drawing of this condition, shows the relation of the parts. On palpation there was no cystocele, and the posterior mass seemed to be continuous beyond the cervical attachment. On rectal examination it did not seem to be rectal in origin. The cervix was somewhat enlarged and superficially eroded. A preoperative diag-

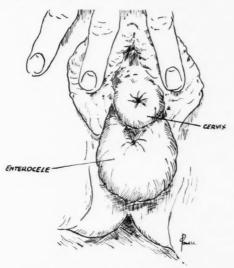


Fig. 1.-Enterocele before operation.

nosis was made of uterine prolapse of moderate or first degree, considerable relaxation of the pelvic floor, and an associated herniation of Douglas' culdesac posteriorly.

On March 2, 1935, the operation was done under local novocaine infiltration anesthesia with absolutely no discomfort to the patient at the time of operation or afterward. The usual perineal opening for a posterior colporrhaphy was made. A dissection of the posterior vaginal wall first from the rectum, then from the anterior surface of the hernial mass using sharp dissection until above the rectovaginal attachment. The more difficult task of dissecting the rectum free from the posterior surface of the sac was then accomplished. The peritoneal sac was isolated from the surrounding fat and fascia and opened, having no contents, it was transfixed as high as possible above the level of the cervix, tied off, and the excess amputated. A high purse-string stitch of the surrounding fascial was done and closed over the stump. A suture grasping the rectovaginal fascial stump on either side was passed through the posterior vaginal wall high up and tied. A high posterior colporrhaphy completed this part of the operation. A high amputation

was done on the cervix. Fig. 2 is a drawing made at the time of operation which demonstrates the anatomic relation of the hernial sac. There resulted a firm perineum with no vaginal protrusion.

Patient died from an embolus of the femoral artery three months later. It was most unfortunate that at the autopsy no examination of these structures was carried out, since only one case of vaginal hernia has been reported at autopsy.

Case 2.—Mrs. P., University Hospital No. 49544, aged fifty-six, gravida v, sixteen years ago the last child was born, all quite normal labors. Menopause at fifty-two years.

Ten years ago she had a sensation of dragging down in the pelvis. Seven years ago she fell off a five-foot ladder, and about this time she first noticed some bulging in the vagina. This gradually increased in size and during the year became

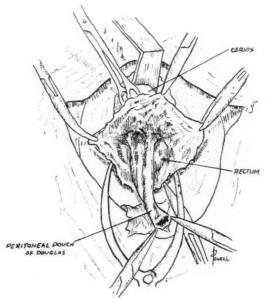


Fig. 2.—Enterocele operation.

much worse, particularly in walking and running a sewing machine so that she had to stop work. The tumor would disappear on lying down. The past year it was hard for her to hold her urine for any length of time.

She had been examined previously by three physicians, each making a diagnosis of a cystocele and rectocele, and one added a prolapse of the uterus. On examination there presented a soft swelling, 7 by 9 cm., that filled the vaginal introitus, and protruded some on straining. There was no decensus of the uterus, and very little of the anterior wall or bladder. The mass could easily be replaced, and then with the examining finger high in the vaginal vault, with the patient straining, one could feel the descent of the mass beginning at the level of the cervix. The cervix and uterus were small and there was no pathology present. There was some prolapse of the urethral mucosa. On rectal examination there was slight pouching into the vagina but apparently no connection with the large mass. A preoperative diagnosis was made of a relaxed perineum with an enterocele and a prolapse of the urethral mucosa.

On March 16, 1935, the operation was done under spinal novocaine anesthesia. The prolapsed urethral mucosa was cauterized radially. The same procedure was carried out in the repair of the hernia and the perineum as was done in the first case. At the end of two weeks there was a firm perineum with no protrusion on straining. A statement from her at the end of four months indicates that there has been no recurrence of her former complaints.

After a review of some sixty cases in the English literature and with this experience of being able to demonstrate the very definite entity of a herniation of the peritoneum of Douglas' culdesac through the perineal floor, it would seem that this condition might be overlooked very easily. It may also account for some of the poor results following a posterior colporrhaphy.

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620 OMAHA LOAN BUILDING

ELLIOTT TREATMENT IN PUERPERAL INFECTION

John H. Moore, M.D., F.A.C.S., Grand Forks, N. D.

(From the Healy, Law, Woutat, Moore Clinic)

THE treatment of an acute puerperal infection is symptomatic and supportive. It must remain so until a specific is found, which seems unlikely when all the varying factors of the infection are considered. Therefore, if any therapeutic procedure seems to have merit in the treatment of such a serious condition as an acute puerperal infection, it should be reported. For this reason, I desire to report three cases of acute puerperal infection in which Elliott treatment gave gratifying results.

All three of these patients had well-defined infections when I first saw them. The first two were classified as antepartum on admission to the hospital, and the third, a patient seen in consultation, had her infection develop within a few hours after the termination of labor.

REPORT OF CASES

Case 1.—St. Michael's Hospital, 32915. Mrs. E. M., white, aged thirty-seven years, gravida iv, para ii. Her previous history was negative except for a spontaneous abortion at three months and an appendectomy, followed by phlebitis of the left leg.

There had been nothing abnormal in this pregnancy until the onset of the present complaint. Her estimated confinement was Aug. 17, 1934. She was admitted to the

hospital on Aug. 14, 1934, with the history that labor pains had occurred one week before but had subsided and that the membranes had ruptured three days before admission.

Her temperature was 100.2° F. and pulse 100 at the time of my first examination and she had had three chills. Her tongue was heavily coated and her breath foul. The uterus extended to the ensiform, was of boardlike rigidity, and the lower uterine segment and both adnexal regions were exquisitely tender to even light palpation. There was a foul-smelling, profuse, yellowish green vaginal discharge. On rectal examination the cervix was found rigid, one-third effaced and the os was dilated to 1 cm. No presenting part could be outlined.

Supportive treatment was instituted and a diagnosis of antepartum sepsis was made.

After a labor of thirteen hours she was delivered of a stillborn male fetus, weighing 9 pounds and showing beginning maceration. A large amount of foul-smelling liquid of pea-soup consistency escaped from the uterus at the beginning of the third stage. Cultures from the uterus showed a bacillus of the colon group and Staphylococcus albus, pyogenes.

Her postpartum condition was not satisfactory. On the second postpartum day her temperature reached 104° F. Elliott treatment was started on the third postpartum day and on the fourth postpartum day she was given a transfusion of 300 c.c. of citrated blood.

Three striking changes occurred in this patient after Elliott treatments were started: (1) The abdominal distention and tenderness subsided rapidly. (2) The lochia became profuse and at first was very foul but after four days of treatment it became normal in amount and the foul odor disappeared. (3) The temperature never went above 100° F. The patient was discharged on her sixteenth postpartum day. At her final examination, three months after delivery, I found involution good, no parametrial thickening or tenderness and, aside from old cervical and perineal lacerations which will require surgery at a later date, her pelvic organs were in good condition.

Her blood culture, taken on admission to the hospital, was negative at the end of two weeks. On admission her sedimentation rate was 80 per cent in the first hour. Her blood Wassermann was negative. The urine at one time showed pus and blood and albumin, Grade 2, but this quickly returned to normal.

She received a total of ten Elliott treatments.

Case 2.—St. Michael's Hospital, 33387. Mrs. W. S., white, aged thirty years, gravida vi, para v, was admitted on Nov. 10, 1934, with the following history: She was approximately at term when, on Nov. 5, 1934, the membranes ruptured spontaneously while she was at home. No pains occurred until the afternoon of Nov. 7, 1934, and no physician was called to attend her until 10 p.m. on Nov. 7, 1934. At that time her physician found her temperature to be 100.6°, and pulse 114. Dilatation was 10 cm. and the face was presenting. She delivered a stillborn female fetus weighing 10 pounds at 12:10 a.m. on Nov. 8, 1934, after her physician had corrected the face presentation. The placenta was delivered by Credè expression ten minutes later, and it was complete. One hour later her physician reported her temperature 103° and pulse 128. She ran a septic course from that time until her admission to the hospital. She had two chills on November 7 and 9 and one chill, which lasted for fifteen minutes, the morning of November 10. Her maximum temperature, prior to admission, was 105.6° F.

On admission her temperature was 101.6° F., pulse 118, respiration 22, and blood pressure 130-64. She had a septic appearance and there was marked circumoral pallor. The tongue was coated and dry. The heart and lungs were negative. There was slight

abdominal distention. Healed appendectomy and cholecystectomy scars were present. The uterus was tender, two fingerbreadths below the umbilicus, and tenderness was very great over the left lower quadrant of the abdomen. The introitus was relaxed. There was moderate thin serosanguineous lochia. The cervix was well contracted and in fair repair and showed the usual early postpartum suggulations. The left parametrium was boardlike and very tender, the right, less so but it showed some involvement.

Cultures from the uterus were reported a pure culture of Staphylococcus albus, pyogenes. Blood culture, taken on admission, was negative after two weeks. The urine examination was negative and the blood Wassermann was negative. Sedimentation rate was 52 per cent the first hour.

Elliott treatment was started the evening of her admission to the hospital and she received a total of six treatments.

She received two transfusions of citrated blood, 300 c.c. each on Nov. 11 and Nov. 14, 1934. She was discharged after eleven days of hospital treatment.

The most noteworthy findings in this case were: (1) The uterine and parametrial tenderness became markedly lessened on the third day of Elliott treatment. (2) The temperature was 101.8° F. when treatment was started and never went above 100.8° F. thereafter.

On examinations Dec. 22, 1934, Feb. 13, and March 6, 1935, the patient was found to have some residual parametrial thickening on the left side, some cervical erosion, and moderate leucorrhea. The uterus was of normal size and in good position. Her menstrual periods had been reestablished and, aside from some increase in the amount of flow, were normal.

Case 3.—Deaconess Hospital, 31861. Mrs. G. S., white, aged nineteen years, gravida i, para i, was delivered of a boy by mid-plane forceps operation by her own physician on April 1, 1935, following a labor of forty-eight hours. Her pulse varied between 100 and 126 immediately postpartum. Three hours after labor her temperature was 101.8° but it reached 104° on April 3, two days after labor.

I saw her in consultation on April 3, 1935, and found a very apprehensive patient with a dusky cyanosis, temperature 103.6° F., pulse 160, and respirations 34. Her blood pressure was 98/66. There was a suspicion of beginning consolidation at the base of the right lung. Both heart sounds were present but of poor quality. The uterus was softer than normal, three fingerbreadths below the umbilicus, and tenderness was marked over the uterus and over the left lower quadrant of the abdomen. Her tongue was dirty and dry. Smears from the uterus revealed organisms which, morphologically and with Gram's stain, resembled the pneumococcus.

Elliott treatment was started on April 4, 1935, and she received a total of ten treatments.

Her temperature reached normal on the ninth postpartum day. Her case was complicated by a well-defined pneumonia which was limited to the lower lobe of the right lung.

Several striking changes occurred in this patient following the institution of Elliott treatment: (1) The lochia, which had been scant before treatment was started, became profuse within forty-eight hours after beginning treatment. (2) Involution progressed rapidly. (3) The temperature and pulse steadily declined.

On April 5, 1935, her sedimentation rate was 50 per cent at the end of one hour. A blood culture was not taken.

DISCUSSION

These three patients were all suffering with acute puerperal infections. They all received the usual supportive treatment of dextrose in normal saline solution by phleboclysis and Cases 1 and 2 received blood transfusions. All of them received

ergot, quinine, and pituitrin. A high carbohydrate diet was employed. B_{0} stasis was treated solely by mineral oil by mouth and tap water enemas when necessary.

On theoretical grounds, one might hesitate to employ Elliott treatment in patients of this type because of the danger of hemorrhage. Hemorrhage did not occur. The marked increase in the lochia in each case after Elliott treatments were started was accompanied by a rapid decrease in the size of the uterus without exception. This seemed to me to be a logical accompaniment of the pelvic hyperemia produced.

The analgesic effect of the Elliott treatments was marked in all three patients. All of them were apprehensive when the first treatments were started and it required a little tactful and patient reassurance to gain their confidence but, after the first treatment, each patient expressed herself as pleased with the relief from pain and tenderness which she experienced. It was a very common thing to have the patients sleep through subsequent treatments. No analgesic drugs were required after Elliott treatments had been instituted except for an occasional dose of codeine.

PERSONAL RECORD OF HYSTERECTOMIES PERFORMED DURING A PERIOD OF FIVE YEARS*

HERMANN GRAD, M.D., F.A.C.S., NEW YORK, N. Y.

DR. REUBEN PETERSON, in discussing the risk of operation in gynecologic cases, states that "Today it is not sufficient merely to examine the urine of a patient to determine whether or not it is safe to operate . . . failure to detect serious diseases of the lungs, heart, liver, and kidneys may result in postoperative deaths."

The operative risk in any case may depend upon many factors: pathologic conditions that call for operative procedure, complications and technical difficulties of the operation, the various organs involved, the physiologic condition of the heart, circulatory and endocrine systems, and other organs. The effect of anesthesia must also be taken into consideration.

At the Woman's Hospital all patients who enter for operation have a thorough physical examination, which includes nose, throat, and teeth, and if necessary, the eyes. The heart and lungs are checked up, as well as the blood pressure. The height and weight are recorded. The laboratory check-up on the urine and blood sedimentation rate, if requested. Smears are taken from the genitourinary tract if needed. Secondary anemias are treated by direct blood transfusions. If the sedimentation test is fast the case is further studied for the possible cause of the same. Consultations are freely held between the members of the staff. The diagnosis, as well as the opinions about the risk of operation of the various consultants are recorded.

^{*}Presented at a meeting of the Section of Obstetrics and Gynecology, New York Academy of Medicine, April 23, 1935.

Borderline cases of anemia are typed before operation, and often a donor is in attendance during the operation ready to be used should the necessity arise for a transfusion.

The patient is safeguarded against chilling of the skin and is encouraged to relax and obtain sleep the night before operation. Operations are postponed if any signs of a cold are present. Cathartics are avoided, but the colon is unloaded by enemas. The patient is encouraged to drink a little more water than otherwise. A preliminary dose of morphine is given before the anesthesia. For many years I have used for this purpose hyoscine and morphine with gratifying results. Hysocine is a powerful cerebral sedative and in combination with morphine, the respiratory tract is less moist, an advantage in inhalation anesthesia. Under suitable conditions avertin is frequently used.

My technic of operation of hysterectomy is very simple. The round ligaments are severed from the uterus, and the cut ends tied to insure safe hemostasis. The peritoneum of the bladder reflexion is opened up and the cervix exposed. If the ovary is to be removed the infundibulopelvic ligament is cut between clamps and tied off in mass. If the ovary is conserved the broad ligament is cut between clamps and the vessels in the uteroovarian ligament tied individually. The uterine arteries are tied with a Grad* ligature. The cervix is cut across and the canal of the cervix is carbolized and touched with alcohol. The stump of the cervix and operative field is carefully peritonized. All raw surfaces are covered with peritoneum. No particular attention is paid to the round ligaments, but they are used for peritonization. If the ovaries are conserved the broad ligaments are sutured to the side of the cervix. In uncomplicated cases the abdomen is closed without drainage. Plain, smallsized gut is used for the peritoneum. In stout women the fascia is closed with figure-of-eight Bauer and Black suture. In other cases the fascia is closed with a continuous mercerized silk. The skin is closed with a subcuticular stitch of silk. The silk sutures in the fascia are tied over a gauze bolster.

Tables I and II show the statistical studies of the cases of hysterectomy done by me in the five-year period.

In married patients sterility in one case of every three. Lowest hemoglobin was 35 per cent, highest 110.5 per cent. Blood transfusion, when necessary, in 18 cases, 7.3 per cent. The highest systolic blood pressure was 190, the lowest 80. Albumin was found in the urine of 71 cases, 28.9 per cent. Menstruation was regular in 154 cases, 62.6 per cent; irregular in 83 cases, 33.7 per cent, and ceased in 9 cases, 3.7 per cent.

There were complete hysterectomies in 51 cases, 20.8 per cent, supravaginal hysterectomies in 195 cases, 79.2 per cent.

There were four deaths, a mortality of 1.6 per cent. Of the 180 private cases there were two deaths, 1.1 per cent, of the 66 ward cases two deaths, 3.3 per cent.

^{*}Note: This method of ligation is described in Am. J. Obst. 79: 379, 1919.

	TABLE I	
First year		49 cases
Second year		42 cases
Third year		42 cases
Fourth year		51 cases
Fifth year		62 cases
Total		246 cases
Private cases	180	73.2 per cent
Ward cases	66	26.8 per cent
Youngest patient		23 years
Oldest patient		56 years
Model age		40 years
	TABLE II	
Unmarried	20 cases	8.1 per cent
Married	226 cases	91.9 per cent
Conceived	162 cases	71.6 per cent

Among the complete hysterectomies there was one death, 1.9 per cent, among the supravaginal hysterectomies (195 cases) there were three deaths, 1.5 per cent,

TABLE III. WOUND HEALING

Primary union	222	cases	90.3	per	cent
Slight disturbance but no suppuration	10	cases	4.1	per	cent
Slight suppuration	3	cases	1.2	per	cent
Considerable breaking down	7	cases	2.8	per	cent
Died	4	cases	1.6	per	cent
Recovered without complication	200	cases	85.4	per	cent

Both tubes and ovaries were removed in 114 cases, 4.6 per cent, one tube and ovary removed in 109 cases, 44.3 per cent, both tubes and ovaries remaining in 23 cases, 9.3 per cent.

Three of these patients died of acute general peritonitis and one died of lobar pneumonia, confirmed by autopsy. In every one of these cases there was pus present at the time of operation. The presence of pus in itself is not of much significance. We have all seen pus cases where the smoothest possible recovery follows the operation. In all these patients that recovered so smoothly with the presence of pus, we must presume that there was an organism present with attenuated virulence, or that the resistance of the patient was such as to overcome the onslaught of the organism.

During a second five-year period I performed 262 hysterectomies among which there were six fatalities, a mortality rate of 2.2 per cent. This seems a favorable mortality rate considering that both Peterson¹ and Burch² in their experience noted a mortality rate of 4.5 per cent.

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A PROTECTIVE SHIELD FOR PROLAPSED CORD

PRELIMINARY REPORT

WILLIAM F. MENGERT, M.D., IOWA CITY, IOWA

(From the Department of Obstetrics and Gynecology, State University of Iowa)

TREATMENT of prolapse of the umbilical cord through the incompletely dilated cervix is unsatisfactory because fetal mortality remains high. Attempts at reposition of the cord generally are futile since it has a continued tendency to prolapse. However, if the prolapsed loop is wrapped in mercurochrome-saturated gauze before reposition, there is less likelihood of recurrence. The insertion of a Voorhees' bag following such attempts at reposition introduces a grave danger of compressing the cord between bag and cervix. Most obstetricians feel that manual dilatation of the cervix with its inevitable lacerations is too radical a method of therapy under such circumstances, while the use of cesarean section, in view of the notoriously poor fetal risk, is seldom justifiable.

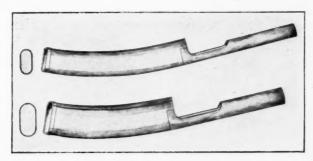


Fig. 1.—Drawing of shields of each size showing shape of cross-section of the tube. The smaller size is $1\frac{1}{2}$ by 3 and the larger 2 by 4 cm. The lengths of the tubes are 17 and 19 cm. and of the handles, 14 cm.

Some device which can protect the prolapsed loop of cord from compression during the first stage of labor without injuring maternal tissues, suggests itself.

A shield has been devised to achieve this purpose. (Fig. 1.) It is essentially a flattened, metal tube, with a pelvic curve and a handle to facilitate manipulation. The lumen must be large enough to admit both branches of the prolapsed loop. In cross-section the tube is rectangular with rounded ends. Shields were made in two sizes, $1\frac{1}{2}$ by 3 and 2 by 4 cm. in cross-section, and in two lengths, 17 and 19 cm. (Fig. 2).

In use (Fig. 2, A, B, and C), a suitable length of umbilical tape is threaded through the shield, through the loop of prolapsed cord, and back through the shield (Fig. 2, B). Gentle traction insinuates the loop of cord into the shield as it is passed up and through the cervix. The shield remains in position until the cervix becomes fully dilated, at which time delivery may be accomplished. If necessary, a Voorhees' bag may be inserted beside the shield to provide a dilating wedge (Fig. 2, C).

The device has been used only once, but the experience was so promising that it is described so that others may utilize it. A detailed protocol of the particular case follows:

L. H., a septigravida, aged thirty-four years, Hospital Number K 11,821, was admitted to the University Hospital May 4, 1935, in the ninth lunar month of pregnancy. The first six pregnancies and labors were normal except that one child was born prematurely. The present pregnancy was also normal. On May 10, 1935, the bag of waters ruptured spontaneously, although only a small quantity of fluid escaped. During the following two days the patient complained of cramping pains in the lower abdomen and back and insisted she was in labor, even though repeated rectal examinations showed only 1 cm. dilatation of the os. At 11:30 A.M., May 13, 1935, sixty-five hours after spontaneous rupture of membranes, the patient noticed something

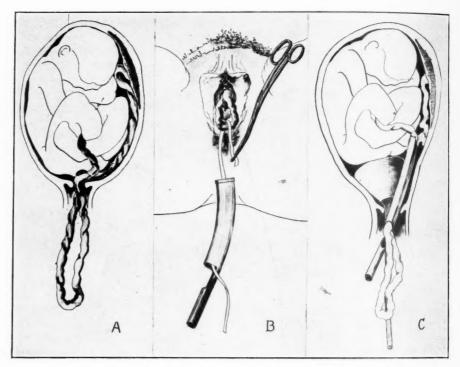


Fig. 2.—Showing method of application of the protective shield. A, Diagrammatic sketch of a cord prolapsed through an undilated cervix. B shows a loop of umbilical tape with one branch threaded through the shield and the other about to be threaded after it has been carried through the prolapsed loop. C, The protective shield and a Voorhees' bag in situ.

at the vulva and called a nurse, who detected the prolapsed cord. At 11:35 A.M., no visible pulsation was evident in the prolapsed loop, the extravulval portion of which was about 15 cm. long (7 to 8 cm. doubled), but at 11:40 A.M. the cord was palpated and a slow, feeble pulsation detected. The short, 1½ by 3 cm., shield was introduced under sterile precautions at 11:46 A.M. without anesthesia. Some difficulty was experienced because the cervical os was still 1 cm. in diameter and required slight digital dilatation. As soon as the shield passed the internal os, visible pulsations, not hitherto observed, became evident and the fetal pulse rate improved slightly.

The fetus lay in L.S.A. (complete breech), was obviously premature, and its heart sounds could not be heard.

When the prolapsed cord was moistened with warm sterile water, its diameter immediately increased 50 per cent and pulsations became stronger. Consequently, the exposed cord was packed in gauze and moistened with repeated applications of hot, sterile, normal saline.

Under light ethylene anesthesia a Voorhees' bag was inserted and filled with sterile water without affecting cord pulsations. A medium size was chosen because it was feared that a larger one might overlap the uterine end of the shield and pinch the cord. The bag was expelled at 12:35 P.M. and was replaced immediately with the largest size available.

At this time, cord pulsations were weak. Two minims of epinephrine were injected into the umbilical vein, but there was no appreciable change in fetal heart rate or strength. The needle caused moderate bleeding which was controlled by slight pressure with the moist pack around the cord.

The second bag, not quite fully distended, was expelled at 1:05 P.M. The patient was immediately anesthetized, draped, given 0.5 c.c. of epinephrine intramuscularly, and breech extraction was begun. This proceeded easily until the head met the incompletely dilated cervix, which was incised about 1 cm. in two places.

The child, which was extracted at 1:10 P.M., was limp and pale, but was revived by tubbing in warm water and by carbon dioxide-oxygen supplied through an intratracheal catheter. It soon breathed independently though rapidly, and obviously was suffering from intracranial hemorrhage. Twenty cubic centimeters of maternal blood were injected under the skin of the back. The baby, a male weighing 2,085 gm., died at 5:30 P.M., four hours and twenty minutes after birth. Autopsy revealed a tear of the left tentorium and cerebellar hemorrhage. No evidences of asphyxia were noted. The cord measured 74 cm. in length.

DISCUSSION

The prompt appearance of visible pulsations in a hitherto pulseless, prolapsed cord, following introduction of the protective shield, indicates that pressure was removed from the cord by the instrument. As a corollary it also appears that absence of pulsations in a prolapsed loop should not deter one from using the shield.

The observed change in diameter of the pulsating, prolapsed cord when moisture and heat were applied is of considerable interest. Inasmuch as the cord was pulsating before, during and after this alteration in diameter, the change was probably due to some vasomotor phenomenon in the cord rather than to alteration in force of the fetal heartbeat. It would seem that maintenance of proper thermic and hygroscopic conditions of the prolapsed portion of the cord is an important part of the therapy.

As experience and knowledge in the use of the shield develop, the injection of epinephrine into the fetal circulation may prove of value. However, it will be used with caution in subsequent cases. The use of alpha-lobelin, a respiratory stimulant, is of course contraindicated until after birth of the child.

The second Voorhees' bag was insufficiently expanded and did not produce full cervical dilatation, which factor surely contributed to the intracranial hemorrhage in the baby. There is, however, no evidence that the presence of the shield interfered with complete distention of the bag.

Despite the fact that the cord protruded through the vulva for one hour and forty minutes, and that the cervix was filled with a Voorhees' bag for one hour of this time, the baby was born alive and breathed spontaneously for four hours. Its death, as proved by autopsy, was due to intracranial hemorrhage with prematurity and breech presentation predisposing factors.

KIRSCHNER-WAGNER OPERATION FOR CONSTRUCTION OF ARTIFICIAL VAGINA*

DAVID N. BARROWS, M.D., NEW YORK, N. Y.

IN CASTING about several years ago for a simple, safe operation for construction of an artificial vagina in a case of congenital aplasia, we were attracted to the Kirschner-Wagner procedure mainly by two factors: no possibility of endangering the patient's life and desirability of a short period of hospitalization.

There are many well-tried and well-established operations for congenital absence of the vaginal canal, but most of them have one or the other of the above objectionable features. Perhaps the most formidable risk is the well-known Baldwin operation from which, as in any bowel resection, there is, of course, a risk of peritonitis or fistula. Masson, at the Mayo Clinic, however, has recently reported a dozen successful results without mortality.

Another objection to this procedure is the fact that secretions from the small intestinal mucosa may irritate the skin about the vulva.

The other main type of operation is that in which flaps of skin are turned up from the surrounding thighs, buttocks and/or abdomen. The best known and most popular of this group is R. T. Frank's operation, which consists of dissecting a flap from the inner side of the adjacent thigh and by several stages forming a tube lined with epithelium which is evidently turned in and sutured in place from below. In this way, a very satisfactory, capacious and well-lined vagina is formed. This procedure has few drawbacks except the prolonged time consumed due to the fact that it must be done in several stages. One other objection to the use of skin flaps from the immediate vicinity of the vulva, which is present in many of the flapformed types of canal, is that hair follicles are not entirely absent from these thick skin flaps and cause considerable annoyance in the artificial passage.

Kirschner and Wagner using the well-known principle employed in constructing a gastrostomy by thin Thiersch type skin grafts, in 1930 worked out the operation we are considering here in the following manner: One of them, a gynecologist, dissected out a considerable aperture and passage between the bladder and rectum into which was introduced the rubber sponge prosthesis, which the surgeon, the other member of the team, had covered with thin Thiersch grafts fastened in place with the skin side inside by fine plain catgut. The resiliency of the rubber sponge was used to keep the grafts in contact with the raw walls of the canal and so left in place eight to eleven days, long enough for the catgut to be absorbed. Drainage was

^{*}Read at a meeting of the New York Obstetrical Society, May 14, 1935.

obtained by insertion throughout the length of the sponge of a rigid stethoscope tube. On removal of the sponge after eight or ten days, most of the epithelium remained in place and formed a suitable flexible epithelial lining for the vagina. Dilators are employed during the first few weeks to aid in avoiding contraction in the diameter of the canal and through them one can see easily how any granulating areas are progressing.

We have found, as have others, that conscientious and frequent dilatation for the first two months postoperative is a very essential factor in obtaining the desired results. Where the patient is married, the matter is taken care of satisfactorily. In several of those mentioned, proper after-care was not possible.

Mechanical difficulty in removing the grafts has been found by many operators and in the more recent cases, many have used a special knife devised by Schepelmann which cuts a wide strip of tissue more easily than the ordinary skin graft knife. Another aid is to stretch the skin more taut on the thigh with a metal spreader or by sewing blocks of wood to the skin and using them for counter traction at either end of the area, from which the grafts are to be removed.

The advantages of this type of operation, as we see it, are (1) no risk of life or serious morbidity, (2) no bad scars left on the skin as in lifting up thick flaps, (3) no prolonged hospitalization, (4) vaginalization of the lining of the canal, (5) no irritating discharges, and (6) simplicity of technic.

Case 1.—E. B., aged nineteen, with a history of lack of menstruation. Occasional attacks of lower abdominal pain of dull character about two days every month. Apparently a normally developed female, hair and breast tissue and female contour not noticeably deficient. Vagina absent, vulva of normal appearance. Pressure with the finger below urethra allowed invagination of the tissues for a distance of 2.5 cm. Laparotomy revealed two normal tubes and ovaries, the inner ends of the tube being attached to the inner ends of the normal round ligaments at the top of the bladder at points about 7 cm. apart. At these junctions, sections were removed from the rounded ends which showed muscular tissue of uterine type. As these two points were elevated, and the posterior bladder wall was made taut, a linear "Y" shaped thickening extended down in the direction of the vulva. The culdesac of Douglas appeared normal posteriorly, but continued forward to the bladder.

A "U" flap was dissected free from the inner side of the left thigh as the first stage of a Frank operation. After a few days, necrosis of the peripheral 7 cm. caused us to change our plans, and a Kirschner-Wagner operation was performed with the aid of Dr. R. P. Wadhams, who cut the skin grafts, using a rubber sponge prosthesis 4 cm. in diameter and 10 cm. in length without a central drainage tube. Dissection of the cavity could not be extended deeper than 8 cm. as the peritoneum of the extended culdesac was reached. Skin grafts were fastened to the sponge with No. 0 plain interrupted sutures and four silkworm-gut sutures were employed to hold it in place. These were removed on the eleventh day as was the sponge. Considerable discharge escaped during the last three or four days which seemed to have been dammed up behind the sponge. Patient was up and around the ward on the fourteenth day, dilatation having been started by that time. On leaving the

hospital, she was given a dilator of hard rubber of rectal type, as a glass one is easily broken, and we discovered at that time that she was not married although she had told us that she was married on admission. Six months later the canal was found to admit 2 fingers for a distance of 6.5 cm., and to have a remarkably healthy lining. Patient complained of very little discharge. Some limitation of elasticity of the vault of the vagina occurred from scar tissue.

Case 2 .- F. S., aged twenty-six, with an absence of vagina, desired to marry. Patient had a single fused kidney discovered on laparotomy several years ago, and entire absence of the vaginal canal. No uterus was present. Female development was quite normal superficially, and her prospective husband insisted on having the operation performed. Patient well-developed adult of distinctly feminine type. Breasts showed no abnormalities. No evidence of any vaginal canal and no depressa. bility of the tissues of the vulva; slight suggestion of a cribriform hymen. Attempted dilatation of this was unsuccessful. Transverse incision between the bladder and rectum to admit three fingers was carrried to a depth of 10 cm. by blunt dissection. A 5 by 12 cm. rubber sponge prothesis, with central drainage of a silk No. 16 French catheter, was covered with multiple skin grafts as in the previous case. sutured in place by four silkworm sutures. Removed with the sponge on the eleventh day postoperative and dilatation started immediately. Patient was discharged on the twenty-fourth day after ten days out of bed with careful instructions as to the use of a dilator. Patient was kept in a little longer than necessary to make certain of the early dilatation. This case has proved 100 per cent satisfactory on physiologic

Of 32 cases reported in the literature including these two, there have been only five poor results mentioned, and in these the canal, or rather, the caliber of the canal, might have been preserved at a satisfactory size by better dilatation.

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130 East Fifty-sixth Street

ARACHNOIDISM IN PREGNANCY

JOSEPH J. HILTON, M.D., LOS ANGELES, CALIF.

M RS. P., para ii, aged twenty-four years, first presented herself for examination on March 25, 1934. Weight 122 pounds and height 63 inches. Blood pressure 115/80. Urine and blood count were normal. Wassermann was negative. Heart and lungs were normal. There were two scars on the abdomen, one in the median line about 8 cm. in length and the other over McBurney's point about 5 cm. in length. The uterus was slightly above the umbilicus and seemed normal in size and shape for the time of her pregnancy. The perineum was relaxed, due to the presence of an old tear from a previous delivery. There was moderate degree of cystocele and rectocele. The cervix showed an old transverse scar with a slight degree of endocervicitis. Pelvic measurements were: interspinous 26 cm., intercristous 28 cm., intertrochanteric 31 cm., external conjugate 20 cm. Outlet: anteroposterior 11 cm., transverse 10.5 cm., posterior sagittal 7.5 cm. Height of sacrum 11 cm.

Past History.—Appendectomy for acute appendicitis in 1921. Tubal pregnancy involving the left tube at seven weeks in 1931. No serious illnesses or history of allergy.

Obstetric History.—Normal delivery on Jan. 10, 1927, full-term, male child, weighing 8.5 pounds. Two miscarriages subsequently, both induced at the second and third months, with no apparent sequelae.

Menstrual History.—First period at thirteen years, every twenty-eight days, moderate flow, with no pain. Some premenstrual irritability with moderately severe headaches the first day. Her last period was Aug. 8, 1933.

Prenatal Course.—The patient was seen at two-week intervals, and on April 25, 1934, her weight was 128 pounds, blood pressure 100/60, urine negative. The fetus was in L.O.A. position; fetal heart tones in the left lower quadrant, rate 136. Moderate degree of diastasis recti.

Present Attack.—On April 28, 1934, at 3:00 p.m. there was a sudden onset of violent vomiting and retching. Severe abdominal pain was accompanied with chills and marked weakness. The vomiting was incessant, at first consisting of stomach contents; later it was mixed with blood and the last was 25 c.c. of pure blood. There was severe pain in the epigastrium and three loose bowel movements. She was seen by me at 8:30 p.m. Her face was ashen, and she presented the appearance of moderate shock. Pulse 140, temperature 96° F., respirations 30, blood pressure 100/50. At this time the vomitus consisted of blood-stained fluid. There were severe abdominal pain and generalized rigidity situated for the most part in the epigastric region. There was tenderness in a small area over the fundus which seemed to be occupied by a fibroid 3 cm. in diameter. The uterus was tetanic, not extremely hard, and about the size of an eight months' pregnancy. Fetal heart tones were in the right lower quadrant, rate 144.

A premature separation of the placenta was suspected, and she was sent immediately to the Hollywood Hospital by ambulance for observation. On her arrival at the hospital she was vomiting, the uterus was tetanic, and the abdominal pain was severe. A blood count showed red blood cells 3,800,000, hemoglobin 76 per cent, white blood cells 33,500, polymorphonuclears 90 per cent, lymphocytes 10 per cent, Schilling, segs. 70 per cent, stabs 18 per cent, juveniles 2 per cent.

Urine examination gave albumin 3-plus, sugar 0, acetone 4-plus, diacetic acid 1-plus, few coarse granular casts, 10 to 16 leucocytes per high power field, with a few red blood cells.

She was given 375 c.c. of 5 per cent glucose in normal saline solution intravenously and prepared for operation, should a definite indication arise. At 10:30 P.M. her condition improved, the vomiting ceased, and the pulse dropped to 120. The temperature was 99° F. The uterus was softer and she began to have rhythmic contractions every two or three minutes. Dr. E. J. Krahulik was called in consultation and examined the patient at 11:30 p.m. At that time there were regular uterine contractions and no rigidity. Rectal examination revealed a cervix 2 cm. dilated; no effacement. The vertex was below the spines. The possibility of premature separation of the placenta was considered but symptoms were not typical. On account of the prematurity and improvement in her condition, it was decided to continue observation. At 1:30 A.M. fetal heart tones were 148, blood pressure 110/78, temperature 100° F., pulse 96, respirations 24. Contractions every two to five minutes. At 2 A.M. the contractions were stronger and they continued throughout the night until 6 A.M., when they ceased. At 8 A.M. the blood count was 21,000, polymorphonuclears 80 per cent, lymphocytes 16 per cent, large mononuclears 4 per cent, Schilling, segs. 42 per cent, stabs 36 per cent, juveniles 2 per cent. Urine, specific gravity 1020, acid, albumin faint trace, 2 to 5 white blood cells per high power field. The fetal heart tones were good. She was placed on a soft diet. She slept well. The following morning the white blood count was 14,950, polymorphonuclears 74 per cent, lymphocytes 25 per cent, eosinophiles 1 per cent, Schilling, segs. 56 per cent, stabs 17 per cent, juveniles 1 per cent. She was dismissed from the hospital May 1, 1934, apparently free from symptoms.

In search for the cause of the unexplained symptomatology, arachnoidism was considered and the patient questioned, since the possibility offered the solution. She recalled having been bitten by a spider two days previous to the onset of her illness. She was cleaning out a closet when she felt something crawling on her breast. After an attempt to remove it she felt a stinging sensation over the upper abdomen. Grasping her clothing she killed a spider, described by her as black, about the size of a nickel, with a red mark on the abdomen (black widow, Latrodectus mactans). Soon after this she noted a large red spot to the left and a little above the umbilicus, and there was itching and slight pain over this area. She thought nothing of the incident until it was recalled by the questioning. She stated that these spiders were numerous in her apartment, especially in the closets and bathroom. Following this information a careful examination was made of the abdomen and a small indurated area was found 3 cm, above and 1 cm. to the left of the umbilicus.

Although the bite had occurred two days previous to the onset of the symptoms, the possibility of there being a delayed reaction because of the pregnant state may be considered, or there might have been another bite unnoticed by the patient.

On May 17, 1934, the patient was delivered of a normal boy, weighing six pounds, two ounces. The labor was normal, the placenta showed no pathologic changes. The purperium was afebrile and uneventful. Observation was continued for the past nine months and she has enjoyed perfect health in that time.

COMMENTS

In a patient with severe abdominal pain, high leucocyte count and atypical symptoms suggestive of an acute abdominal condition, arachnoidism should be considered, especially since the black widow spiders seem to be increasing in numbers and distribution.

1052 WEST SIXTH STREET

ACROPARESTHESIA

MAX M. GOLDBERG, M.D., NEW ORLEANS, LA. (From the Department of Medicine, Touro Infirmary)

A CROPARESTHESIA is a very common symptom during the climacteric period. In fact, Borak¹ claims that it is a constant symptom of this period. A great number of women suffer slightly with this symptom during the menopause and pay little attention to it, while in a few patients it assumes major proportions as a presenting symptom and causes the patient to seek relief.

The literature regarding this syndrome is barren. There have not been a dozen papers written concerning it in the past twenty years.

Wechsler² describes acroparesthesia as "an ill-defined syndrome which occurs mainly in women at about the climacterium, though artificial menopause is also capable of giving rise to it. Precipitating factors, such as infections, pregnancy, exertion and exposure to cold are predicated on quite fortuitous grounds. The symptoms are mainly subjective in nature and consist of various dysesthesias. The patient complains of numbness and coldness of the extremities, especially of the finger tips, of tingling and crawling sensations. Pains are occasionally present. The hands are stiff and need limbering up. The condition is practically constant, but considerably worse at night and toward morning. There are no objective signs as a rule. Occasionally one observes pallor of the fingers and slight diminution of sensation."

"Acroparesthesia has been divided into two groups by Strauss and Gutman: one, a vasoneurosis occurring between the ages of twenty and forty, characterized, in addition by cyanosis, blanching, or edema of the fingers; the other, occurring at the menopause, and resembling tetany, with exaggerated electric and mechanical irritability of nerves, but without vasomotor symptoms. The clinical picture develops gradually, runs a chronic course for years, and ultimately disappears."

No attempts to treat the acroparesthesias endocrinologically have been recorded either in the textbooks or in the literature. In view of the evident close association of the syndrome with the menopause, it was felt that an attempt to treat these symptoms with the estrogenic hormone would be indicated. Other menopausal symptoms were studied in conjunction.

The estrogenic hormone (theelin, Parke, Davis and Company) was used in doses of 300 rat units injected subcutaneously once a week. This dosage will usually bring symptomatic relief to the average patient suffering from menopausal symptoms. In two patients other substances, as indicated, were used.

Twenty cases form the basis for this report. Two patients were treated with theominal (Winthrop) tablets, one tablet after each meal. Both patients obtained almost complete relief from the acroparesthesia and also the vasomotor flushes, and are included to indicate that substances other than hormones may be successfully used to counteract the symptoms.

Of the eighteen remaining patients who received theelin, sixteen were greatly relieved of both the vasomotor flushes and acroparesthesia within two to four weeks after the institution of treatment. In no case was the acroparesthesia completely controlled, a slight amount persisting. In four cases the acroparesthesia had been so severe as to awaken the patients once or twice during the night. All four of these patients were able to sleep through the night and awaken in the morning with only slight symptoms, following the use of the hormone.

In one patient, in whom an artificial menopause had been induced with radium three years prior to the onset of this treatment, and in whom the vasomotor flushes and acroparesthesia were severe, no relief was obtained even after using 300 rat units twice a week for four weeks. Relief might have been obtained with much larger doses, but these could not be obtained because of the cost. Another patient, in whom a surgical menopause had been induced four years previously, and in whom vasomotor flushes, acroparesthesia, and allergic (hay fever, mild asthma) symptoms occurred simultaneously in May of each year since, received slight relief from 300 rat unit doses administered twice weekly.

SUMMARY

A small series of cases (twenty) is presented in which acroparesthesia was prominent as a symptom and evidently associated with the menopause. Treatment with theominal in two cases, and estrogenic hormone in sixteen cases produced almost complete relief.

In one case, following artificial menopause induced by radium, no relief was obtained. In another case, following surgical castration, only slight relief was obtained

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TORSION OF THE HYDATID OF MORGAGNI SIMULATING EARLY RUPTURED ECTOPIC PREGNANCY

I. Tractenberg, M.D., Brooklyn, N. Y.

(From the Gynecological Clinic of Unity Hospital)

THE case herein described is reported because it is extremely rare and simulated an early ruptured ectopic pregnancy.

Mrs. H. B., a well-developed female, twenty-nine years of age, was admitted, by ambulance, to the hospital, with complaints of acute abdominal pain in the lower left quadrant. She appeared very ill upon admission.

Her menses began at the age of thirteen, lasting four days, recurring about every three months, accompanied by severe pain. She married at the age of twenty and was married eight years when the symptoms of acute condition of the abdomen came on. After her marriage, her periods became regular, of the twenty-eight-day type. Two years later she was delivered of a normal child. Her pregnancy and parturition were normal in every respect. She felt well up to three years ago when her periods began to become irregular and again were accompanied by dysmenorrhea.

About two months before her admission to the hospital the pain increased in severity and was accompanied by nausea and vomiting. It was aggravated by walking and greatly relieved by rest. On the day she was admitted to the hospital she experienced a sharp agonizing cramplike pain in the lower abdomen with nausea and vomiting.

Her temperature when admitted was 101.2° F., pulse 120, and respiration 28.

Physical examination revealed a distended abdomen, which was tender, more so to the left quadrant. There was also rebound tenderness.

Vaginal examination revealed a small mass in the left fornix. It was freely movable and very tender to the touch. There was a brownish bloody discharge from the vagina.

The blood count showed white cells 13,500, with 80 per cent polymorphonuclears,

red cells 3,800,000, 65 per cent hemoglobin.

A tentative clinical diagnosis of ectopic pregnancy of the left side was made because there was a history of two months' amenorrhea, a palpable mass on the left side, pain was felt upon pushing against the cervix, and there was a bloody discharge from the vagina.

Six hours later a laparotomy was performed through a midline incision. A blood-tinged serous fluid was found in the abdominal cavity. The left tube was red and congested, the fimbria end was found to be edematous, and hanging from the fimbria by a pedicle 3 cm. long, with two complete twists. There was a dark red cystic mass, the size of a small tangerine (4 cm. by 3 cm.). It was a hydatid cyst of Morgagni. No other pathology was found in the pelvic cavity.

The cyst was removed and the patient made an uneventful recovery.

Histologic Findings: The cyst was lined with a single layer of low cuboidal cells. The vessels in the wall were necrosed and there was some hyalinization. The content of the cyst was a bloody serous fluid.

From a survey of the literature on the subject I could find only one case similar to this one, namely that of Dr. Waters,1

Besides this there are three others of torsion of the hydatid of Morgagni reported,² but these occurred on the right side and simulated acute appendicitis.

My case, however, differs from that of Dr. Waters in that it occurred in a married woman. It differs from the others in that it occurred on the left side, and, principally, because it simulated an early ruptured ectopic pregnancy as the patient was married and gave a history of irregular menstruation.

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514 OCEAN PARKWAY

AN UNUSUAL CASE OF POSTPARTUM INFECTION

IRVING B. KRELLENSTEIN, M.D., F.A.C.S., NEW YORK, N. Y.

THIS patient, admitted to Lebanon Hospital, died six hours after a normal delivery with a temperature of 104° F., which could not be accounted for at the time.

The patient was a para ii, twenty-eight years old, had typhus fever many years ago, had a normal spontaneous delivery about three years ago. Her menses began when she was thirteen years old, were always regular, twenty-eight-day type, and would last about three to five days. Her last period was Jan. 26, 1934. She first appeared at the prenatal clinic of Lebanon Hospital on July 11, 1934.

She had experienced no trouble during this pregnancy, except for mild morning sickness of short duration, constipation, and slight leucorrhea. Prior to her pregnancy she developed an abscessed tooth which was not treated. Physical examination disclosed an obese woman about five and one-half months pregnant; otherwise nega-

tive. Blood pressure during the pregnancy ranged between 90/60 and 110/60. Urine was negative for sugar and albumin. Blood chemistry and Wassermann tests were not done.

The first stage of labor began on Oct. 14, 1934, at 7.30 A.M. Membranes had ruptured a few hours prior to the onset of pains. The pains at this time were fairly effectual. The second stage began at 2 P.M. of the same day. Pains were strong and occurred every three minutes. At 5:10 P.M. the patient developed a chill of thirty minutes' duration; no anesthesia was used for the spontaneous delivery which occurred at 5:17 p.m. Placenta was delivered at 5:35 p.m. She had a slight laceration of the perineum which required two stitches. Bleeding was normal. At 6:15 P.M. she became flushed and developed a rectal temperature of 104° F., pulse rate of 160, and respirations of 25 per minute. At 7 P.M. she began to bleed moderately and because of her general condition and the fear of serious hemorrhage, the uterus was packed and the bleeding controlled. At 8 P.M. she went into shock, but reacted to the usual therapy which included an intravenous 5 per cent glucose in normal saline. At 11 P.M. she vomited brownish fluid and then rested quietly until 12 M., when she suddenly became cyanotic, dyspneic, and very restless; the pulse became very weak and thready. Repeated stimulation failed to improve the pulse and the patient died at 1 A.M. on Oct. 15, 1934. Just before she died she regurgitated a profuse amount of brownish fluid from her mouth and nose.

A postmortem was performed by Dr. Joseph C. Ehrlich. There were no petechial hemorrhages and no peripheral edema. On opening the abdomen there was no evidence of peritonitis or free fluid in the peritoneal cavity. The stomach was markedly dilated and the intestines were not distended. The right heart was markedly dilated, the wall increased in thickness; the wall of the right ventricle showed an increase in fat, the left auricle was normal in size. The left ventricle was slightly dilated and the wall was of normal thickness. The general appearance of the heart muscle was of a grayish pink color, with pale streaks. It was soft in consistency and presented the appearance of a marked parenchymatous degeneration. The lungs showed areas of congestion and pulmonary edema. The liver weighed 1,400 gm., and had a pasty appearance and was exceedingly pale. A mass the size of a golf ball, which on section presented a yellow appearance, was present in the right lobe posteriorly. This was a large hepatoma which did not present any distinguishing features microscopically. The kidneys weighed 280 gm. and revealed the picture of parenchymatous degeneration. Both kidneys showed dilatation of pelves and calyces. There was marked congestion of the mucosa of the pelvis. A thick greenish exudate was found in the pelvis which on culture revealed a Streptococcus hemolyticus. The spleen weighed 275 gm. and appeared congested and of a semifluid consistency, typical of a septic spleen. Culture here also revealed Streptococcus hemolyticus. The uterus, tubes, and ovaries showed nothing pathologic.

The cause of death was acute cardiac failure, caused by parenchymatous degeneration and an underlying septic process, the cause of which was undetermined. One might suspect that there was some connection between the abscessed tooth and the sepsis.

2021 GRAND CONCOURSE

Special Article

CONTRACEPTION, STERILIZATION, AND HYGIENE OF MARRIAGE IN THE MEDICAL CURRICULUM

THE REPORT OF A SURVEY CONDUCTED BY THE NATIONAL COMMITTEE ON MATERNAL HEALTH, INC.*

REPLIES to a questionnaire sent by the National Committee on Maternal Health, Inc., in 1933 to the seventy-six Grade-A medical schools listed by the American Medical Association in 1932, are here reported and commented upon.

The following letter was written to each Dean:

"Growing interest in the medical control of fertility is shown by the increase in contraceptive clinic services, from twenty-eight in 1928 to one hundred and twenty in 1932; by provision in twenty-seven states for sterilization (without unsexing) of the insane and feebleminded; by instruction in contraception or sterilization in more than thirty medical schools (1930); and by endorsement of such teaching by certain medical groups.

"We would welcome a statement of your point of view and that of your faculty on the desirability of teaching medical students the indications for and technic of contraception and of sterilization. Have you been able to take steps in this direction? Have legal restrictions, traditions, and local public opinion had a bearing on the matter? If such teaching has been started, please outline the content and method.

"May we learn your viewpoint on a third matter? It is coming to be recognized that much infelicity in marriage arises from inadequate understanding of its physical and mental aspects, and that medical students leave their schools poorly prepared to help their future patients in this respect. Do you consider instruction in the hygiene of marriage to be possible or desirable? If so, should it be part of preventive medicine or gynecology-obstetrics?

"We believe that it will be of considerable interest to medical educators and to the profession generally, to have the consensus of opinion of the deans of the medical schools, and your cooperation in this direction will be greatly appreciated. While we hope that you will wish to answer at length, we enclose a short form for your convenience."

Replies were received from 62 of the 76 medical schools. Forty-seven deans or heads of gynecologic departments not only made out and signed the formal question-naire, but wrote accompanying letters. Nine of the 76 schools offer only the two-year preclinical course; 67 give clinical instruction. Five of the 67 are under Roman Catholic control, leaving 61 which might instruct in contraception and sterilization. Of these, 59 sent replies, upon which this report is based.

The returns showed that a majority of the Grade A schools were giving some sort of instruction in the medical control of conception. Both sterilization and contraception were taught, though in different departments and in different ways.

^{*}The officers of the Committee: Dr. Haven Emerson, Chairman, Board of Directors; Dr. Robert L. Dickinson, Chairman, Executive Committee; Dr. Frederick C. Holden, Director; Dr. Howard C. Taylor, Jr., Secretary; Dr. Clarence J. Gamble, Treasurer; Dr. Raymond Squier, Executive Secretary.

In many schools where neither contraception nor sterilization was being taught the deans believed that instruction in the subjects should be given. The overcrowded curriculum was usually assigned as the reason for not including the subjects in the regular course of instruction. There were few instances where disapproval was expressed.

Interest in the field was not confined to any section of the country. The South is usually considered very conservative, but answers to our questionnaire showed that it was as progressive, in this respect, as the North or West. The greatest conservatism was displayed in schools in states where the laws were most restrictive; and in one school in the East it seemed to have been thought better, after consultation with various members of the faculty, not to commit the institution to anything, by leaving the questionnaire unanswered.

Thirty schools reported no contraception teaching, though some were planning for it, and approved it in principle. Table I shows the total number of schools teaching either subject, and the method of instruction. No details were given by the deans, nor were the number of lectures or textbooks used indicated.

TABLE I. METHOD

	AND CLINIC	LECTURE ONLY	CLINIC ONLY	UNSPECI- FIED	TOTAL
Contraception	12	11	2	3	28
Sterilization	16	9	4	2	31
Not teaching contraception but teaching sterilization Not teaching either subject	_	_	_	glandige glandige	8 20

In the schools where contraception was taught, 25 gave the instruction in the Departments of Obstetrics or Gynecology, 1 in the Department of Social Hygiene and Criminology, 1 in the Department of Preventive Medicine and Clinical Demonstration, and 1 was unspecified. One school taught only the danger of the use of certain devices, and so was not included in the list.

The schools teaching sterilization gave their instruction as follows: 22 in the Departments of Obstetrics and Gynecology; 4 in the Departments of Obstetrics, Gynecology and Urology; 3 in the Department of Surgery; 1 in the Department of Preventive Medicine and Clinical Demonstration; and 1 was unspecified.

One school, which taught by lecture only, referred patients to an extramural clinic in a health center for contraceptive advice, while those eligible for sterilization were referred to state institutions. The dean in this school considered, however, that both types of care should be given in the medical school clinics themselves.

COMMENTS AND OPINIONS

The Committee's inquiry was intended both to sound out opinion and to count the schools teaching the subjects in question. The returns in 1933 showed a difference from reports of five years ago or earlier. There have been decided changes not only in public opinion, but also in the field of medical jurisprudence, as evidenced by such legal decisions as that of the United States Supreme Court (Justice Holmes) affirming the constitutionality of the law for eugenical sterilization in the Virginia case of Buck vs. Bell.² Also, there have been many favorable judicial interpretations of the obscenity laws.

Interesting though they are, it is not possible to quote from the deans' letters. Many of them realized the restrictions of the law; but while these laws restricted instruction in many medical schools, there was no instance in which medical clinics

properly directed or instructing medical students had been interfered with by the Government, nor had texts and materials been barred from the mails or common carriers. Although state and federal laws on this subject remain unchanged, so far as the practice of medicine is concerned they are not enforced, but they always constitute a potential danger.

The third inquiry in our questionnaire, which covered marriage counsel, was the one to which the largest number (42) replied. Of these, 32 considered such teaching practicable; 38 desirable. On the negative side three did not consider it practicable and four did not regard it as desirable. Almost everyone who wrote was in accord with the idea that such instruction should be given in the medical school, that it was of great importance to the student, and that it would be of much help to him as he went out into practice; but many deans were of the opinion that there was no one in their particular school who was fitted to give such teaching. One or two said they were going to try out a series of lectures with the hope that some instructor might be developed who would be able to carry on the work. Many deans wrote that they knew of no adequate texts in the field* and so had attempted nothing further than lectures and assigned readings, but were not at all satisfied that all possible was being done. However, there are adequate books of instruction and source books available, as listed in the footnote appended to this report.

Recommendations for graduate and undergraduate instruction in control of fertility have been made by such groups as the New York Academy of Medicine³ and the Committee on Obstetric Education of the White House Conference on Child Health and Protection.⁴

SUMMARY

From the replies received to all the questions submitted to these medical schools on the teaching of contraception, sterilization, premarital examination and the hygiene of marriage some general conclusions may be drawn:

- 1. Many of the Grade A medical schools are including both contraception and sterilization in their courses of instruction to students. No school appears to have laid out a definite course in either subject as part of its curriculum. The subjects are taught by occasional lectures or clinical instruction or both, and usually in the Senior year.
- 2. Comparison of replies received by S. Adolphus Knopf in 1929 and 1930⁵ and by the National Committee on Maternal Health in 1933 shows a small gain in the number of medical schools giving information and instruction in the field of contraception and sterilization, more particularly that of sterilization.
- 3. The marked interest shown by deans of medical schools in the questions of premarital instruction and the hygiene of marriage indicates a growing feeling that these subjects are important and ought not to be neglected.

^{*}Good books written by physicians, some for physicians, some for a wider range of readers, include the following: For medical practitioners: Dickinson-Bryant: Control of Conception, Baltimore, 1931, Williams and Wilkins; Kopp: Birth Control in Practice, New York, 1934, McBride; Matsner: Technique of Contraception, Baltimore, 1934, Williams and Wilkins; Voge: The Chemistry and Physics of Contraceptives, London, 1933. Cape. Factual books, for physicians: Davis: Sex Factors in the Lives of 2,200 Women, New York, 1929, Harper: Dickinson: Human Sex Anatomy, Baltimore 1933, Williams and Wilkins; Dickinson-Beam: A Thousand Marriage, Baltimore, 1931, Williams and Wilkins; Dickinson-Beam: The Single Woman, Baltimore 1934, Williams and Wilkins; Hamilton, Gilbert V.: A Research in Marriage, New York, 1929, Boni. For readers not necessarily medical: Ellis: Psychology of Sex, New York, 1933, Long and Smith; Everett, M. S.: The Hygiene of Marriage, New York, 1932, Vanguard; Exner: Sexual Side of Marriage, New York, 1932, Norton; Folsom, Joseph K.: Family, New York, 1934, Wiley; Groves, Ernest R.: Marriage, New York, 1933. Norton; Wright: Sex Factor in Marriage, New York, 1931, Vanguard; Dickinson: The Doctor as Marriage Counsellor (soon to go to press) Baltimore, Williams and Wilkins.

If centers for marriage counsel are started, emphasis at first should not be on service to the maximum number of couples, but on intensive study and follow-up of individual clients. Beginnings in this field have been made already in many parts of the country, and we can look to the experience of these centers to round out and improve our present tentative methods.

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Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 14, 1935

The following paper and case reports were presented:

A Résumé of 223 Cases of Surgical Sterilization. Dr. Clifford B. Lull, Philadelphia, Pa. (By invitation.) (For original article, see page 101.)

Kirschner-Wagner Operation for Construction of Artificial Vagina, 2 Cases. Dr. David N. Barrows. (For original article, see page 156.)

Report of a Case of Tubo-Ovarian Pregnancy. Dr. William T. Kennedy,

Mayer, I.: Experiments and Clinical Results of Ovarian and Uterine Grafts, Rev. franç. de gynéc. et d'obst. 29: 827, 1934.

Experiments on dogs and clinical experience lead Mayer to the belief that autografts of ovarian tissue should be utilized systemmatically among all women under fifty years of age who have to have both ovaries removed. It is important to graft fragments from the superficial portions of the ovary and to handle these pieces of tissue very gently in order not to destroy the germinal epithelium and the underlying primordial follicles. Autografts of uterine tissue in subcutaneous cellular tissue readily take, and the resulting uteroovarian hormones have a distinct effect on the development of the ovarian grafts. In cases where a subtotal hysterectomy is performed it is useful to add a uterine graft to the ovarian one. It is effective, simple and without danger.

J. P. GREENHILL.

American Journal of Obstetrics and Gynecology

EDITORS: GEORGE W. KOSMAK, M.D., AND HUGO EHRENFEST, M.D. ASSOCIATE EDITORS: HOWARD C. TAYLOR, JR., M.D., AND WILLIAM J. DIECKMANN, M.D.

Comment

The Premature Infant

THE Premature Infant Station of the Michael Reese Hospital in Chicago, the Institute of Juvenile Research in Chicago, and the Behavior Research Fund jointly undertook a study of the fate of the prematurely born infant as compared with that of his brothers and sisters of full-term birth. The results of this exhaustive research recently have been presented in a volume entitled *The Physical and Mental Growth of Prematurely Born Children.*¹ This title does not indicate or even suggest that it contains much new information of great interest and practical value to the obstetrician.

The Committee on Factors and Causes of Fetal, New-Born and Maternal Morbidity and Mortality of the last White House Conference (1930), in a special report on Birth and Death Certificates, suggested that "Prematurity" be defined as the birth of a viable fetus after the twenty-eighth week of uterine gestation and having reached at least 35 cm. from crown of head to base of heel with body fully extended; a fetus being considered premature up to 260 days of uterine gestation with a birth weight less than 2,500 grams and length less than 45 cm. --- "Before the twenty-eighth week a fetal death should be recorded as an abortion."

Obviously these definitions simply gave expression to views generally held at that time. The estimation of the "actual duration of uterine gestation" of necessity can be only an approximate one and is subject to inescapable inaccuracies, chiefly because it is based on the usually uncomfirmable statement of the mother in regard to the date of her last menstruation. Therefore, in general, more often the birth weight now is accepted as a more reliable indicator of the degree of prematurity. It seems that the chances of survival for an infant

^{&#}x27;The Physical and Mental Growth of Prematurely Born Children. By Julius H. Hess, M.D., George J. Mohr, M.D., Phyllis F. Barthelme, Ph.D. The University of Chicago Press, Chicago, Ill. 1935.

weighing less than 2,500 gm. are assessed as so small and insignificant, that at present in the majority of published statistics on intranatal and neonatal fetal mortality the deaths of infants below this weight are regarded as justifiably deductable from the total loss.

Can this custom be continued in the light of certain facts revealed in these newer studies? Considering the figures of results only for the last three years, 1931, 1932, and 1933, we find:

YEAR	UNDER 1000 GRAMS	1000- 1500	1500- 2000	2000- 2500	ABOVE 2500	TOTAL ADM.	LIVED	DIED	LIVED
1931									
Lived	0	25	63	72	7	207	167	40	80.7
Died	9	17	7	7	0				
1932									
Lived	2	16	70	86	9	249	184	65	74.0
Died	5	26	28	9	0				
1933									
Lived	5	25	78	48	4	208	160	48	76.9
Died	10	14	17	7	0				

In this tabulation we have a total of 646 infants weighing between 1,000 and 2,500 gm., of whom 490 survived, which represents almost 76 per cent. It seems fair to assert that the obstetrician cannot any longer, for statistical or any other purposes, coolly deny all responsibility for the death of a newborn infant below 2,500 gm. It would be impossible to outline here the relatively simple means by which such truly astonishing results have been achieved. In the main they must be ascribed to the immediate institution of appropriate care which obviously thus has to be supplied by the physician present at birth. However, at least one emphatic statement of Dr. Hess shall be quoted: "A most important period in the life of the premature infant is the time between birth and the institution of some proper method for the prevention of thermal shock. Many of these infants are lost through carelessness in protecting them during the first hours after birth."

These investigations also provide much new information in regard to the relation of intracranial birth injury of the premature infant either to his early death or to later physical and mental deficiencies. Between 1922 and 1934, 350 autopsies were made on babies weighing more than 1,000 and less than 2,500 gm. The pathologic records show 167 instances of intracranial hemorrhage and 8 birth injuries of other types. Furthermore, "in 21 cases autopsy was not permitted, but it was felt that clinical evidence and findings on spinal puncture warranted a diagnosis of intracranial hemorrhage." Thus in this large series, intracranial injuries had caused the death of approximately 40 per cent of prematurely born babies alive when admitted to the service. The total loss from intracranial traumatization, including the stillborn infants and those dying before admission, of course was

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much larger. Official statistical figures, calculated merely from death certificates, always run much lower. Many explanations for this fact easily suggest themselves, but one, of particular significance in this connection, is the fact that no health officer will question the diagnosis "prematurity" as direct cause of death if the infant's weight is given as below 2,500 gm.

It has been pointed out repeatedly that in general, especially by neurologists and pediatricians, the importance of birth trauma in the causation of physical and mental defects is exaggerated. Unfortunately most investigations along these lines have been made in institutes for feebleminded or crippled children, a preceding birth injury being assumed most often merely on the assertion of the mother that she had a very difficult labor. Reliable data in regard to the relationship of birth to later defect can be obtained only with the aid of exact observations made on the newborn by the physician within the first few hours or days of life. From this point of view the researches made on the Chicago material are of particular importance. Among the 987 infants finally discharged from the Premature Infant Station, 102 had been considered as having sustained intracranial damage. Sixty-nine of them have been under close observation and have had from one to four physical examinations or psychometric tests. A little more than 75 per cent of these 69 infants had been born between the thirtieth and thirty-sixth week of gestation, all of them weighed less than 2,500 gm., and as a matter of fact, 45 per cent of them between 1,500 and 2,000 gm., almost 30 per cent between 1,000 and 1,500 gm.

At the time when investigations for this report were ended, 42 infants showed no evidence of brain injury, 11 evidence of severe, 7 of moderate, and 9 of slight damage. Of the 11 severely injured with marked paralytic and spastic symptoms, 7 showed mental retardation. The same observation of mental deficiency was made in 4 of the group of 7 with moderate traumatization at birth. In the last group of 9 with only slight evident damage, 6 were of average intelligence, 2 were retarded, and 1 was classified as "superior." In several of the cases the signs of a resulting defect became manifest only later in life.

Of late, repeatedly the claim has been made that in premature infants subsequent deficiencies are more likely to be due to imperfect development of the central nervous system at the time of birth. Such an argument is considerably weakened by this follow-up made on prematurely born infants who immediately after birth had exhibited suggestive or unmistakable signs of intracranial traumatization. It seems that these new, expertly made observations rather prove that there was no exaggeration in the statement of Vaglio (1921), that the notoriously high mortality of premature infants probably is due rather to the trauma of birth than to immaturity; or in the assertion of Ylppoe, that the fate of the prematurely born infant is chiefly deter-

mined by the degree of its traumatization in birth. The shape of the soft and elastic cranium of the prematurely expelled fetus is easily and often too quickly altered to a dangerous and disastrous degree. The obstetrician should ever keep in mind that such exaggerated change in configuration can also be effected by the resistance of soft portions of the birth channel, by a not completely dilated cervix, a rigid perineum, or a narrow vulva ring. The obstetrician in the management of a premature labor must refrain from all medication or obstetric measures which tend to hasten the passage of the head and should never hesitate to make a required episiotomy in a primigravida.

Incidentally, this report will convince every obstetrician that duplication of the model Premature Infant Station of the Michael Reese Hospital in every large city would effect a considerable lowering of present infant mortality rates.

HUGO EHRENFEST.

Theobald, G. W.: An Account of Obstetric Methods at St. Mary Abbots Hospital, Kensington, Brit. M. J. 2: 850, 1934.

In this article the author describes the arrangement of an obstetric and gynecologic unit in a general hospital supervised by himself, and discusses the rules and regulations governing the admission of patients to various sections of the unit, as well as the actual management of the labor ward, the uncomplicated delivery, the difficult case, and the puerperium.

In summarizing his findings, the author states: (1) Over 800 patients were confined without resorting to cesarean section or to induction of labor in the treatment of contracted pelvis or of the toxemias of pregnancy. Twelve out of thirteen infants were born spontaneously with the occiput in the posterior position. The forceps rate was under 3.5 per cent. (2) The morbidity rate was, it is believed, the lowest recorded by any hospital in the country. (3) The methods used in the labor ward can be carried out in any tenement dwelling in the country, no sterile gowns, towels, masks or stockings being required. (4) A maneuver for estimating whether a head can pass through the pelvis is described. (5) It is suggested that rendering the urine alkaline during the puerperium by administration of potassium citrate is of importance in preventing morbidity. (6) A technic for preventing mastitis and breast abscess is given. (7) The value of the prophylactic use of antistreptococcal serum is stressed. (8) Maternal mortality would be lessened if midwives were not allowed to make vaginal examinations. (9) The increasing maternal mortality rate must be attributed to increased operative intervention. If the present policies are continued, a still further increase may be anticipated during this decade.

F. L. ADAIR AND I. C. UDESKY.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Collective Review

THE ESTROGENIC, CARCINOGENIC, AND ANTERIOR PITUITARY GROWTH PRINCIPLES, AND THEIR CLINICAL RELATION TO BENIGN AND

* MALIGNANT TUMORS

J. THORNWELL WITHERSPOON, M.A. (OXON), M.D., NEW ORLEANS, LA. (From the Department of Gynecology, Tulane University, School of Medicine)

CLINICAL interest in the relationship between the estrogenic and carcinogenic principles has been intensified by the fact that certain substances which produce animal carcinoma are somewhat similar chemically to the estrogenic hormone, and even produce estrous changes.¹ The molecular structure of the estrogenic and carcinogenic compounds, 1-2-benzpyrene, 5-6-cyclopenteno-1-2-benanthracene and 1-2-5-6-dibenzanthracene, which are nonsaturated hydrocarbons possessing the tricyclic phenanthrene ring, is very similar. The actions of these principles are also somewhat alike as each exhibits growth promoting properties, involving epithelial tissue primarily; their actions differ, however, in that the estrogenic hormone is essentially a sexual growth stimulating factor, affecting especially the female genital tract and the mammary glands, while the action of the carcinogenic agent is growth stimulation of any and all body tissue.

Loeb² has excellently demonstrated a comparison of these two principles and has drawn the conclusion that (1) there are substances which are both carcinogenic and estrogenic; (2) there are carcinogenic substances which are not estrogenic; (3) there are estrogenic substances which are not carcinogenic; and (4) even in cases in which the compounds are both estrogenic and carcinogenic, there is no parallelism between the strength of their activities.

In 1931 Dodds³ issued a warning, "I do not think that the amazing potency of theelin (the estrogenic hormone) is recognized by the majority of cancer research workers. It is capable of producing the most extensive tissue proliferation and cell growth, and this appears to me to be of the utmost importance." Administration of the estrogenic hormone results in hypertrophy and hyperplasia of only and all the female secondary sexual organs including the breasts, while castration (lack of the estrogenic principle) in female mice under six months of age leads to marked retardation of the rate of growth of mammary cancer, but does not prevent the experimental production of cancer by carcinogenic agents.⁴, ⁵ The effect of castration is greater the earlier it is done. If castration is performed after the tumor inoculation, retardation of growth is not as effective.⁶ Castration, however, has no effect on the growth of animal sarcoma⁷ and skin cancer.⁸ This undoubtedly is due to the fact that the estrogenic principle is only a sexual growth stimulating factor

and is not a general body stimulating agent. This limitation of estrogenic activity to only secondary sexual tissue, breast, uterus, vagina, and tubes, explains the conflicting results reported concerning its action in experimental cancer; yet full cognizance of such is not generally recognized. The estrogenic hormone stimulates the rate of growth of experimental mammary cancer, and may even produce breast cancer in mice⁹ (this observation has neither been repeated nor confirmed), yet its action is ineffective on the rate of growth of animal sarcoma and skin cancer. It is this specific and limited character which distinguishes the action of the estrogenic hormone from the carcinogenic factor.

Burrows¹⁰ failed to demonstrate a carcinogenic action of the estrogenic hormone by applying it directly to the skin of mice over a long period of time; this method has been found effective with the carcinogenic hydrocarbons of tar. There is at present no evidence for the origin of carcinogenic compounds developing in the animal body from the estrogenic hormone.¹¹ Loeb, however, has demonstrated the interaction of certain cancer hereditary factors in mice and the estrogenic hormone acting as a stimulant to tissue growth as the igniting factor for mammary cancer, the most frequent tumor in this species.²

As far as the etiology of cancer is concerned, the carcinogenic compounds, acting as growth stimulants, may induce malignant growth formation without first causing local irritation or tissue hypertrophy.² Nor are these compounds selective as to the substratum in which they act, since they produce epithelial cancer when applied directly to the skin of the animal over a long period, and sarcoma when injected subcutaneously. The agents apparently effect changes in the cells on which they act, and these changes ultimately result in cancer formation from originally normal cells.

UTERINE FIBROIDS

Recent investigations on granulosa cell tumors, associated with disturbances in the available supply of the estrogenic hormone, have reflected precocious development of the secondary sexual organs in young girls.¹² Also multiple follicle cysts of the ovary, with no corpora lutea, and apparently excess estrogenic activity, have been found associated consistently with endometrial hyperplasia and uterine fibroids.¹³ In view of the close relation between the carcinogenic and estrogenic principles, this seems particularly significant.

That stimulation by the estrogenic hormone causes myometrial hypertrophy and hyperplasia has been frequently noted. Dodds, 14 Clauberg, 15 and others have produced uterine enlargement in women, from infantile to adult size, by the administration of large doses, 500,000 to 1,000,000 R.U., of the estrogenic hormone. Only clinical observations, since uterine fibroids are comparatively rare in the lower animals, have warranted the hypothesis that if estrogenic stimulation is prolonged sufficiently, uterine fibroids will develop, in addition to myometrial hyperplasia. In several former communications,13, 16-18 from a clinical and pathologic study the relationship of endometrial hyperplasia and increased activity of the estrogenic hormone, in the absence of any corpora lutea influence, was noted. At the same time it was suggested that the myometrium was also affected by the excessive estrogenic action, especially so in view of the fact that this stimulation was abnormally great. A further hypothesis was advanced: if this estrogenic activity was prolonged sufficiently, because fibroids are slow growing tumors, the result would be (1) immediate endometrial changes characterized by hyperplasia, and (2) more latent myometrial pathology as uterine fibroids. The clinical and pathologic data on 283 cases of uterine fibroids were presented to substantiate this hypothesis. Lewis and Geschickter19 have demonstrated the presence of the estrogenic principle in a uterine myoma.

Because the molecular structure and growth promoting properties of the estrogenic and carcinogenic principles are so similar, and because of the clinical association of

uterine fibroids and excessive estrogenic activity, it may possibly be concluded that increased and prolonged stimulation on the myometrium by the estrogenic hormone will subsequently result in uterine fibroid formation.

ENDOMETRIOMAS

Endometriomas are also under the influence of the estrogenic hormone. Their morphologic and functional characteristics are similar to the uterine endometrium; the integrity and function of endometriomas are dependent upon the presence of active ovarian tissue, since castration causes regression of the tumor; they present decidual reaction during pregnancy, and undergo the rhythmic endometrial changes of the menstrual cycle.

Since the estrogenic hormone is the cause of endometrial hyperplasia, and since the histologic structure of endometriomas and uterine endometrium are similar, it is logical to deduce that the igniting growth factor of endometriomas, which brings about cellular metaplasia or endometrial implant proliferation, is the estrogenic principle. That such is the case is all the more established by the fact that many endometriomas present histologically endometrial hyperplasia, and also by the high incidence of association of endometriomas with uterine endometrial hyperplasia. The frequent finding of all the features of endometrial hyperplasia in the endometriomas, accompanied by similar changes in the uterine mucosa, can only be caused by the factor which definitely determines the latter, the estrogenic hormone.

BENIGN AND MALIGNANT TUMORS OF THE BREAST

The stimulating and growth promoting action of the estrogenic hormone is the main factor in mammary development at puberty. Watson has demonstrated marked breast development in a nineteen-year-old hypogonadal amenorrheic girl who was given the estrogenic hormone in 500,000 R.U. doses, and Geschickter and coworkers,20 while investigating the action of this hormone upon breast hypertrophy and tumor formation, conclude that gynecomastia in the male and virginal hypertrophy and fibroadenoma in the female breast are dependent upon pathologic variations in the action of the estrogenic hormone upon the duct epithelium and surrounding breast tissue. These observers have demonstrated the presence of the estrogenic principle in a fibroadenoma of the breast.

Since the growth rate of mammary cancer in animals is accelerated by the estrogenic principle, and since breast hypertrophy and benign tumor formation in human beings are influenced by this hormone, it seems logical to conclude that human breast malignancy may also be affected by the action of the estrogenic hormone. In the treatment of mammary malignancy, therefore, estrogenic activity should be removed, since its presence may be an exciting growth factor.

In carcinoma of the breast in women under the menopausal age, estrogenic activity is generally not destroyed, and it continues to exert its growth stimulating effect on the, if any, remaining cancer cells. In addition, therefore, to surgery, in the treatment of cancer of the breast in women who have not reached the menopause, all ovarian activity and secretion should be removed either by radium or deep x-ray therapy. Induction of the menopause, especially in young women, in the treatment of carcinoma of the breast may seem somewhat radical, but in view of the tremendous growth promoting action of the estrogenic principle on sexual tissue, this treatment is very rational. That elimination of estrogenic activity may be beneficial in the treatment of malignancy of the breast in women who are still in their functional years could possibly be demonstrated by an analysis of a series of five-year cures of cancer of the breast before and after the menopause. If elimination of estrogenic activity is beneficial in the treatment of mammary malignancy, there should be more cures of this condition in postmenopausal women, discounting of course the age element and the extent of the malignancy.

CANCER OF THE FEMALE GENITAL ORGANS

The activity of the estrogenic hormone as a growth promoting agent on the female generative organs is similar to its action on the mammary glands. In malignancy of the genital viscera, therefore, estrogenic activity should be eliminated, and this usually is the case. In cancer of the cervix sufficient dosage of radium is used to induce cessation of all ovarian and estrogenic activity. Also in malignancy of the fundus, the uterus, tubes, and ovaries are generally removed and thus the estrogenic element is destroyed. In ovarian carcinoma the estrogenic hormone activity is probably ineffective as a growth stimulant, since this organ is not under its direct influence. Surgery and deep x-ray therapy to the ovaries, however, will usually remove its effect. On the other hand, cancer of the vulva, when treated surgically, should have the estrogenic activity removed, similar to its elimination in mammary malignancies.

CANCER AND THE ANTERIOR PITUITARY GROWTH FACTOR

That the anterior hypophyseal growth promoting principle plays an important rôle on the growth rate of animal malignancy has been repeatedly demonstrated. Many observers,21-24 have produced in animals retardation of carcinoma and sarcoma growth rates by hypophysectomy. If hypophysectomy is performed after the development or implantation of the tumor, there is an immediate reduction in the neoplastic growth rate, but no complete cessation of growth occurs. This operation also leads to cessation of body growth. If hypophysectomy is done two or three weeks before inoculation, the retardation of growth is most effective. On administering the anterior pituitary growth principle to these hypophysectomized animals, the tumor and body growth rates are immediately increased.

Zondek²⁵ and others,²⁶ using the antagonistic relationship hypothesis between the anterior pituitary growth and sex factors,²⁷ have inhibited animal malignancy growth rates by administering the pregnancy urine hormone.

Bischoff^{24, 28} has demonstrated that after sublethal pituitary irradiation the rate of growth of rat sarcoma 10, rat carcinoma 256, mouse carcinoma (spontaneous mammary) and mouse sarcoma 180 is significantly retarded, but the effect is observed only when body growth is virtually arrested. Moreover, the effect on the tumor growth rate is transient, and massive dosages of irradiation are required to produce the necessary retardation of body growth. In animals whose body growth weights are arrested by poisons, no retardation effect was noted on the tumor growth.

On the other hand, the increased effect of the growth promoting principle of the anterior lobe on three of the above tumors was marked (the difference between the tumor growth of dosed and controlled animals equaling three times the joint standard deviation of the mean). This effect of the growth promoting principle was less marked in sarcoma than in carcinoma bearing rats and mice.

If the retardation of body and tumor growth rates, following pituitary irradiation, is due to inhibition of activity or lack of production of the anterior hypophyseal growth factor, the administration of this growth principle to animals so treated should result in an acceleration of both body and tumor growth rates. Bischoff²⁴ produced this accelerating body and tumor growth rate effect on rats with carcinoma 256 by daily administering the growth promoting principle, after the animals had been given extensive pituitary irradiation.

Attempts to paralyze permanently the function of the anterior lobe of rats or mice by pituitary irradiation were unsuccessful.²⁴ Even repeated doses of x-ray failed, except in a few cases, to arrest the weight growth curve of these animals. Histologically the effect is quantitative, with only fragments of the anterior lobe remaining, which always present normal appearing cells in regions of débris. In young animals sex impairment is profound. That pituitary irradiation does not completely destroy sex function is demonstrated by a normal course of gestation

in some of the irradiated animals, and by the normal ovarian reactions after the administration of the pregnancy urine hormone.

If any clinical observation can be gleaned from these animal experiments, it is the possible irradiation of the human pituitary gland in cancerous patients, in addition to surgery or local radium treatment. Rodent cancer is a far jump to human cancer, and the majority of experimental animal cancer is tested on fairly young animals when the growth stimulating factor is active, while human cancer tends to occur in elderly patients, when the anterior pituitary growth principle should be relatively inactive, although Wyeth²⁹ and others have shown increase in weight of the anterior hypophysis in cancerous patients, due to proliferation mainly of the eosinophile (growth) cells.

The possible beneficial effects of pituitary irradiation, in paralyzing and repeated doses, to all carcinomatous and sarcomatous patients as well as to genital and mammary malignancies, in addition to elimination of the estrogenic activity, can only be speculated upon. The application of this treatment to cancerous patients, superimposed upon the local therapy of surgery or radium, will have to be tested over a fairly long period of time and then checked against a series of nonirradiated pituitary cancerous cases. The very encouraging results, from animal pituitary irradiation, however, seem to justify such an investigation.

In theory, pituitary irradiation should be more beneficial in checking human malignant growth rates than those in young animals. Clinical cancer generally develops when the patient's growth weight is stationary or even declining, a factor necessary to obtain the tumor growth retardation effect in animals. Even human prophylactic pituitary irradiation of noncancerous menopausal or postmenopausal patients may have its place.

As Bischoff points out, the most important question is whether the anterior lobe growth principle functions alone in accelerating tumor growth or whether another pituitary mechanism induces retardation of tumor growth. From the experiments of the anterior hypophyseal replacement therapy, in which administration of the growth promoting principle counteracted the effect of pituitary irradiation, both in regard to body and tumor growth, it seems most probable that the growth principle of the anterior pituitary gland is both a body and tumor growth accelerating factor.

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Selected Abstracts

Pathologic Puerperium

Paine, C. G.: The Etiology of Puerperal Infection, Brit. M. J. 1: 243, 1935,

Hemolytic streptococci cause the greater number of puerperal infections. The author describes a mode of study of droplet infection and concludes that the organism is conveyed to the patient by the hands of the attendant, direct spraying from nose and throat, or by patient's own hands. The obstetric attendant may carry infection from some other case, by the hands harboring hemolytic streptococci in a trivial lesion, by the hands soiled from pocket handkerchiefs, or by his hands being infected through low momentum droplets from his own throat,

Precautionary measures consist in masks of suitable thickness being well secured under the chin and a rigid hand technic. Masking should be done before any preparations for operation are begun. Bacteriologic control of eases is stressed. Carriers should be guarded rigidly.

F. L. ADAIR AND S. A. PEARL.

Horn, L. L.: Etiology of Puerperal Fever, Monatschr. f. Geburtsh. u. Gynäk, 95: 43, 1933.

In the opinion of Horn, coitus is to be restricted during the first three months of pregnancy since it may cause an abortion. It must be entirely eliminated after the eighth month because it may not only start labor pains in primiparas but may directly cause rupture of the membranes in multiparas and thus lead to premature labor. Coitus just before labor endangers the pregnant woman because there have been reported instances of puerperal sepsis as the direct result of intercourse at this time. In some instances death resulted. The author reports three cases of severe puerperal sepsis observed in the Breslau clinic in all of which the causative factor was coitus just before labor.

J. P. GREENHILL.

Contardo, G. B.: The Bacterial Flora and the Bactericidal Action of the Lochia of the Normal Puerpera, Folia gynaec. 30: 557, 1933.

From a careful study of lochia Contardo concludes that their bactericidal action is greatest during the first two days after delivery. As the bactericidal action diminished he observed the ascension of germs from the vagina into the uterus. In the normal puerpera he found the following organisms predominating: Döderlein's bacillus, Staphylococcus albus and aureus, streptococcus, nonhemolytic type, saprophytic forms.

He does not believe that these organisms cause puerperal infection, but does believe that their growth and ascension are inhibited by the lochia.

J. M. PIERCE.

Martland, H. S.: Puerperal Infection, Am. J. Surg. 26: 90, 1935.

The problem of puerperal infection is almost entirely anatomic, depending on anatomic pathways for its spread, on physical and mechanical phenomena of

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stasis and drainage, on cellular reactions called forth for defense, and has very little to do with fancy theories of immunity or selective affinity of certain strains of bacteria for certain tissues.

Septicemia, in many of these cases, is only intermittent. Bacteria do not multiply and grow in the blood, but are discharged into it from primary or secondary depots, usually in an intermittent fashion. When thrown into the circulating blood, nature makes every effort quickly to rid the blood stream of their presence through its organs of elimination and filtration. The application of chemotherapy in intravenous injections of mercurochrome, gentian-violet and other like substances, is only excusable on the premise of attempting to kill those organisms circulating in the blood at the time of the injections, and thus to prevent the establishment of secondary foci in other parts of the body. As one is unable to know when the blood is being showered, the hopelessness of such procedure seems convincing.

While the anatomic view of the subject leads immediately to the possibility of radical surgery in its eradication, the obvious difficulty in knowing how far the process has extended, greatly restricts surgery to incision and drainage of localized collections of pus, and to rare cases where either the immediate ligation of thrombosed vessels or a quick hysterectomy for a uterus containing multiple abscesses might be seriously considered.

J. THORNWELL WITHERSPOON.

Clason, S.: The Necessity for Strict Isolation of Septic Cases, Acta obst. et gynec. Scandinav. 14: 289, 1934.

The author carefully investigated the deaths which occurred in his hospital in Stockholm with special reference to cases of sepsis observed not only post-partum but also postabortal. He found abundant evidence to support the view that septic abortions cannot be treated in a lying-in hospital without occasioning a certain amount of danger to recently delivered women unless there is complete isolation of the septic cases.

J. P. GREENHILL.

Stähler, F.: Report of One Hundred Eighty-Seven Cases of Puerperal Sepsis and Pyemia Observed During Twelve Years at the Frankfurt Women's Clinic, Monatschr. Geburtsh. u. Gynäk. 99: 193, 1935.

Among 187 cases of puerperal sepsis and pyemia 63.6 per cent were cured. In 139 cases the clinical picture was that of pure pyemia. In this group 68 per cent were cured.

Among 16,704 labor cases the mortality for puerperal sepsis was 0.024 per cent and the morbidity 0.17 per cent. The number of chills does not seem to have any special significance in cases of sepsis. In three cases ligation of pelvic veins was performed but all three women died. The author collected from the literature reports of 32 cases of ligation of pelvic veins with 9 recoveries. He compares the best results obtained with operative procedures (63 per cent) with his 68.2 per cent of cures by conservative therapy, and outlines the treatment employed in this large series of cases of puerperal sepsis. A large number of drugs were used and therapeutic measures carried out, including the injection of metals such as silver, gold, copper, iron, and mercury, chemicals such as arsenic, bismuth, iodine and sulphur; colloidal preparations, and dyes such as methylene blue, trypaflavin, rivanol, etc. However, all of these substances were sooner or later given up. The author found that serum therapy when given early helped in some cases. Blood transfusion was of distinct help. During the last few years

sepsis cases were given blood from pregnant women and good results were obtained. Other measures employed were injection of the patient's own blood, injections of glucose, of insulin and of alcohol. The author will continue his expectant treatment in the future.

J. P. GREENHILL.

Batisweiler, J.: The Significance of Chills in the Prognosis of Puerperal Fever, Monatschr. f. Geburtsh. u. Gynäk. 95: 56, 1933.

Batisweiler points out that chills are frequently the first symptoms of septic infections of genital origin. They may be used to differentiate the various forms of septic processes, they may furnish the indication for surgical measures such as ligation of veins, and above all they may be used for the prognosis of the individual case. The number of chills is significant. If a patient has only one to three chills, the prognosis is favorable, for the mortality is low. Beginning with the fourth chill, the death rate rises suddenly. The time of onset of the first chill is significant. Usually the first chill occurs in the first week after delivery. It begins early in cases where there will be a large number of them. Hence the later the first chill sets in, the better the outlook. The more rapidly the chills recur, the worse the prognosis. The more days which intervene between the chills, the better the chances for recovery. The longer fever lasts after labor or abortion without the occurrence of chills, the more infrequent are the latter. The morbidity is greater in operative cases than in those who have spontaneous deliveries, and abortions stand about midway between these two.

J. P. GREENHILL.

Menzel, U.: Metastases in Puerperal Sepsis, Monatschr. f. Geburtsh. u. Gynäk. 99: 204, 1935.

The author studied a series of 218 cases of puerperal sepsis of which 127 ended fatally and 188 were complicated by metastases. The latter figure indicates the very high incidence of metastases in cases of puerperal sepsis. Practically every organ in the body may be the site of metastases in cases of sepsis. The organs chiefly involved were the lungs, kidneys and the heart in the order named. The most common organisms found were the Streptococcus hemolyticus, the staphylococcus, and the gas bacillus. It is important to recognize the responsible organisms in order to form a proper prognosis. The three organisms just named lead to death in most cases. The author maintains that the hemotogenous route for metastases is more rapid, more frequent, and more fatal than the lymphatic route.

Every metastasis, regardless of how it arose or in which organ it is situated, is an abscess or an area of necrosis. Metastases occur with equal frequency in sepsis following either abortion or full-term labor.

J. P. GREENHILL.

Gocke, H.: Hemorrhages in the Puerperium, Monatschr. f. Geburtsh. u. Gynäk. 94: 154, 1933.

Among 5,371 labor cases there were 41 cases of puerperal hemorrhage. Thirty-eight of these occurred in 5,144 full-term labors and 3 among the 227 premature labors. Fifteen hemorrhages occurred early and 26 late in the puerperium. No hemorrhages were due to cervical lacerations or retained pieces of placenta. The causes of the puerperal bleeding were lacerations of the vagina (4), atony and subinvolution (29), placental polyps (4), endometritis (2), and myoma (1).

The most common cause for the bleeding was atony and subinvolution and the responsible factors for this were age, parity, constitutional anomalies, general debility, fixation operations on the uterus, overstretching of the uterus as in polyhydramnion, large child, abruptio placentae, and operative, very rapid but also very slow emptying of the uterus. Other factors were disturbances in the third stage of labor, fever and infectious processes in the genitalia during the puerperium.

In ten cases, the uterine cavity had to be explored. In four cases, nothing was found but the stimulation had a beneficial effect and the bleeding ceased. No complications were observed as a consequence of these manipulations.

J. P. GREENHILL.

Kochmann, G.: Blood Transfusion in Cases of Puerperal Sepsis and Secondary Anemia, Monatschr. f. Geburtsh. u. Gynäk. 93: 154, 1933.

At the Danzig clinic it has recently been the custom to treat all the severe cases of puerperal sepsis systematically with blood transfusion. No ill effects have been observed from this procedure. The benefits are: (1) In many cases of sepsis there is an anemia and this is overcome rapidly by the transfusion; (2) In cases of sepsis there is a diminution in the protective ferments, antitoxic and antibacterial properties of the blood and these are replaced by the transfused blood; (3) The transfused blood improves the circulation which is usually depressed by sepsis; (4) The injected blood acts as a strong stimulus to the defense mechanism of the body against infection. Of 16 seriously ill septic patients treated by means of blood transfusion 11 died and 5 recovered.

Blood transfusion is also indicated in cases of secondary anemia as a result of loss of blood from the genitalia. Such bleeding occurs in women with myomas and metropathies and after labor and abortions.

In the opinion of the author blood transfusions should be used much more frequently than they are at the present time, both as a prophylactic measure and therapeutically in cases of severe loss of blood during and after labor.

J. P. GREENHILL.

Serdukoff, M. G.: The Actual Therapy of Puerperal Fever, Gynécologie 33: 622, 1934.

The author outlines his treatment of puerperal fever as follows: For cases of circumscribed parametritis, adnexal inflammation, and thrombophlebitis, he advises rest in bed, ice bags, oxytocic drugs, umbilical cord blood, autohemotherapy, local immunization, and narcotics. If there is no suppuration, he inserts ichthyol tampons in the vagina, gives hot baths under electric lamps, vaccine therapy, and hypodermic injections of turpentine. Where suppuration is present, he incises and drains by means of a posterior colpotomy. In severe cases he resorts to blood transfusions.

He employs specific therapy in the form of intravenous injection of alcohol, umbilical cord serum, blood transfusions, roentgen ray therapy, and fixation absesses. In mild cases he advocates intravenous injections of urotropin, calcium chloride, distilled water, and silver nitrate.

J. P. GREENHILL.

Item

American Board of Obstetrics and Gynecology

The next written examination and review of case histories of Group B applicants for certification by this Board will be held in various cities of the United States and Canada on Saturday, March 28, 1936. Group B applications must be filed in the Secretary's office not later than February 28, 1936.

The oral, clinical, and pathological examination of all candidates for certification by this Board will be held in Kansas City on Monday. May 11, and Tuesday, May 12, 1936, immediately prior to the scientific session of the American Medical Association. Applications for Group A candidates must be received not later than April 1, 1936.

The annual informal dinner and general conference of Diplomates attending the American Medical Association convention will be held at Hotel Kansas Citian, Kansas City, Missouri, Wednesday, May 13, at 7:00 P.M. At this dinner the successful candidates from the examinations of the two preceding days will be presented in person. and short addresses will be made by several members of the Board.

For further information, booklets, and application blanks, apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

LIST OF DIPLOMATES LIMITING THEIR PRACTICE TO OBSTETRICS AND / OR GYNECOLOGY To Date, Sept. 1, 1935

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BENNETT, A. E., CLEVELAND
BILL, A. H., CLEVELAND
BONIFIELD, C. L., CINCINNATI
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HOERNER, J. K., DAYTON
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KRIGBAUM, R. E., COLUMBUS
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MOWRY, F. S., CLEVELAND
PIERCE, J. M., CINCINNATI
REYCRAFT, J. L., CLEVELAND
ROBISHAW, A. W., CLEVELAND
ROBISHAW, A. W., CLEVELAND
ROGERS, ANDREWS, COLUMBUS
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WEIR, W. H., CLEVELAND

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BARNARD, E. P., PHILADELPHIA
BEHNEY, C. A., PHILADELPHIA
CARROLL, J. H., PITTSBURGH
CARROLL, J. H., PITTSBURGH
CARROLL, J. H., PITTSBURGH
CLEMMER, LEON, PHILADELPHIA
CONTI, E. A., PITTSBURGH
CRAIG, E. B., PHILADELPHIA
EISAMAN, J. R., PITTSBURGH
ELY, W. C., PHILADELPHIA
FISHER, J. M., PHILADELPHIA
FISHER, J. M., PHILADELPHIA
GILLIS, R. A. D., PITTSBURGH
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JAMES, D. B., PHILADELPHIA
JAMES, J. E., JR., PHILADELPHIA
KATZ, DAVID, PITTSBURGH
KEENE, F. E., PHILADELPHIA
KIMBROUGH, R. A., JR., PHILADELPHIA
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LAWS, G. M., PHILADELPHIA
LONGAKER, DANIEL, PHILADELPHIA
MACFARLANE, CATHERINE, PHILADELPHIA
MACFARLANE, CATHERINE, PHILADELPHIA
MACFARLANE, CATHERINE, PHILADELPHIA
MACER, CHARLES, PHILADELPHIA
MALER, R. W., PHILADELPHIA
MOHLER, R. W., PHILADELPHIA
NORRIS, C. C., PHILADELPHIA
NORRIS, C. C., PHILADELPHIA
NORRIS, C. C., PHILADELPHIA
PARKE, W. E., PHILADELPHIA

^{*}Deceased

REEVES, T. K., PITTSBURGH SCHEFFEY, L. C., PHILADELPHIA SCHUMANN, E. A., PHILADELPHIA STEVENSON, J. W., PITTSBURGH STEVENSON, J. W., PITTSBURGH
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TAYLOR, J. S., ALTOONA
TITUS, PAUL, PITTSBURGH
TRACY, S. E., PHILADELPHIA
TRUMPETER, J. H., BEAVER
VAUX, N. W., PHILADELPHIA
WILLIAMS, E. F., ALTOONA
WILLIAMS, P. F., PHILADELPHIA

RHODE ISLAND

APPLETON, PAUL, PROVIDENCE HALE, F. S., PROVIDENCE MATTEO, F. I., PROVIDENCE

McCrady, R. L., Charleston Wilson, L. A., Charleston

TENNESSEE

TENNESSEE
BLACK, W. T., MEMPHIS
BURCH, L. E., NASHVILLE
LEWIS, M. S., NASHVILLE
PRIDE, W. T., MEMPHIS
REINBERGER, J. R., MEMPHIS
RING, H. H., COOKEVILLE
RUCH, W. A., MEMPHIS
SCHREIBER, P. C., MEMPHIS
*TOOMBS, P. W., MEMPHIS

TEXAS

BOURLAND, J. W., DALLAS
COOKE, W. R., GALVESTON
GROGAN, R. L., FORT WORTH
HANNAH, C. R., DALLAS
MAXWELL, W. W., SAN ANTONIO
PASSMORE, B. H., SAN ANTONIO

ROBINSON, H. R., GALVESTON SACHER, C. B., DALLAS

VERMONT

EASTMAN, O. N., BURLINGTON

ANDREWS, C. J., NORFOLK BAUGHMAN, GREER, RICHMON GRAY, B. H., RICHMOND RUCKER, M. P., RICHMOND THORNHILL, P. E., NORFOLK WILLIAMS, T. J., UNIVERSITY RICHMOND

WASHINGTON

Bell, W. W., Seattle Thompson, G. G., Seattle

WEST VIRGINIA

BLOSS, J. R., HUNTINGTON

WISCONSIN

CAMPBELL, R. E., MADISON DARLING, F. E., JR., MILWAUKEE DAVIS, C. H., MILWAUKEE HARRIS, J. W., MADISON HORWITZ, J. J., MILWAUKEE

CANADA

CANADA
CANNELL, D. E., TORONTO
*CLELAND, F. A., TORONTO
HARRIS, L. J., TORONTO
HENDRY, W. B., TORONTO
*LITTLE, H. M., MONTREAL
SCOTT, W. A., TORONTO
SHUTE, E. V., LONDON
VAN WYCK, H. B., TORONTO

SYRIA

DORMAN, H. G., BEIRUT

Erratum

On page 893, December, 1935 issue (discussion of Novak's paper), at the beginning of the last paragraph on the page, Carey Culbertson's name has been omitted, thus crediting the entire discussion to Robert T. Frank.

The discussion remarks beginning with "The first suggestion offered by Dr. Novak _ _ _ '' and ending on next page where Novak closes, should be credited to Culbertson.

